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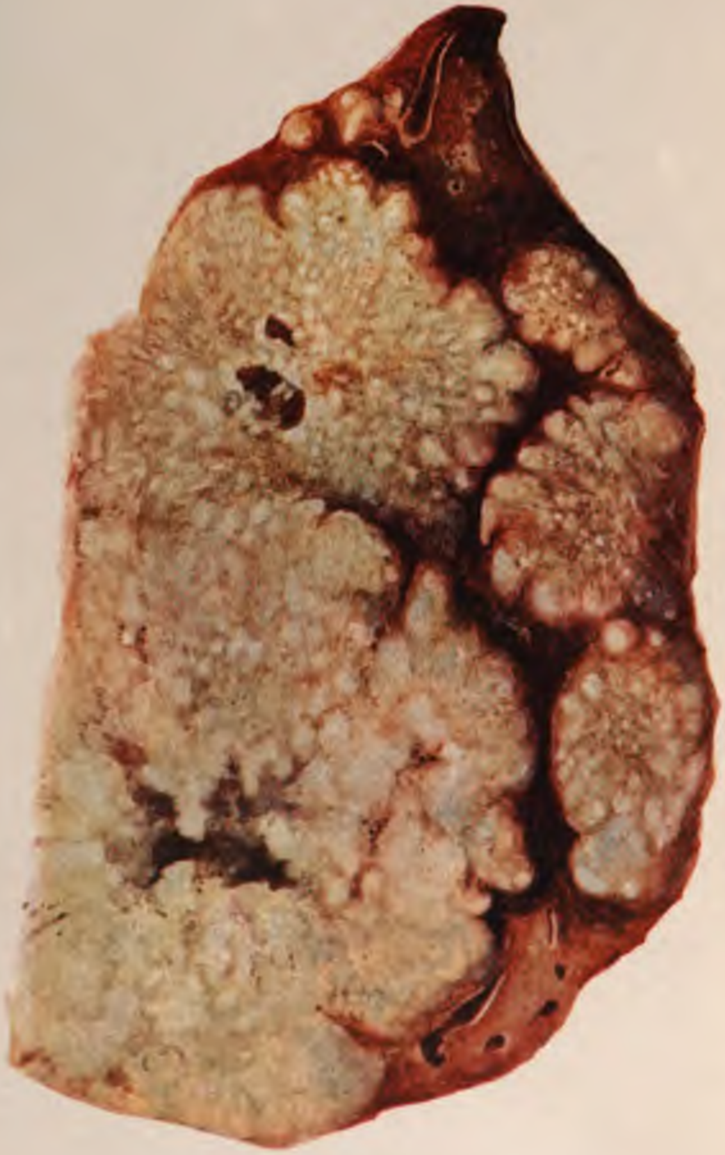

GROWTH IN LIVER SECONDARY TO CARCINOMA OF THE RECTUM.

DISEASES

OF

THE LIVER

GALL-BLADDER AND BILE-DUCTS

BY

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PREFACE.

During the past twelve years I have paid special attention to the diseases of the liver, both from the clinical and pathological points of view. Some of my observations have already appeared in various medical journals, Transactions of Medical Societies, and in articles on diseases of the liver in Vols. V and VI of the Encyclopædia Medica (in 1900).

Special Treatises often begin by dealing with the normal anatomy and physiology of the part concerned, but to be of any real value or use to the reader the anatomy and physiology of the liver must be dealt with in such detail as would seriously add to the bulk of the work, and I have therefore decided to omit any introductory chapter of this kind. I have done so with less regret as I believe that in most instances readers refer to text-books or special monographs on the anatomy and physiology of the subject rather than to the introductory remarks at the commencement of a clinical treatise.

In the description of each disease attention is first directed to the underlying morbid changes as without a grasp of these it is impossible to make a rational diagnosis, to treat the clinical manifestations in a satisfactory manner, or to give a reliable prognosis. Selected cases, for many of which I am indebted to my colleagues at St. George's Hospital, have been embodied in the text, especially in the parts dealing with the symptoms and clinical aspects. These cases and in most instances statistical details have been set in smaller print. The literature of the subject is enormous and though no trouble has been spared, it is inevitable that omissions must exist. After full consideration I have decided to omit, in almost all cases, the bibliographies which had been prepared and have only retained the references to authors actually quoted.

The illustrations are nearly all original and I must cordially acknowledge my gratitude to many past students of St. George's Hospital for their help in this respect, especially to Dr. E. A. Wilson and Mr. Lawrence Jones (coloured plates, etc.), to Dr. H. Spitta and Mr. S. G. Penny (photo-micrographs), and to Messrs. P. L. and S. P. Mummery, Dr. G. H. Goldsmith, and Mr. H. G. Drake Brockman. To Dr. H. Morley Fletcher, Professor S. Delépine, and Dr. T. Fisher I am indebted for permission to use or to copy figures which have already appeared elsewhere.

H. D. Rolleston,

November, 1904,
London, W.

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DISEASES OF THE LIVER
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DISEASES OF THE LIVER.

ANATOMICAL ABNORMALITIES.

ABNORMAL LOBULATION.

The liver is sometimes divided up into a number of lobules so as to suggest a faint resemblance to the condition seen in some animals. This lobulation, which is not homologous to fœtal lobulation of the kidneys, is more marked on the surface of the larger right lobe than on the left lobe. As many as 16 lobules have been found. (Moser.[*]) While these lobules must be distinguished from irregularities and hobnails of portal cirrhosis and from cicatrices manifestly syphilitic, it is probable that this lobulation is due to pathological conditions and is not a morphological phenomenon. It may be due to syphilis, fœtal peritonitis, or possibly to tuberculosis.

Probably in many of the cases syphilitic hepatitis of congenital origin is responsible for the change, but positive evidence to this effect is very often wanting. When lobulation of the liver is associated with peritoneal adhesions, it is possible that peritonitis during fœtal life has modified or interfered with the growth of the organ so as to lead to fissuring and lobulation of its surface.

The view that lobulation of the liver might be caused by poisons manufactured by the Bacillus tuberculosis was put forward by Hanot,[†] who examined seven cases of lobulated livers in patients dying with tuberculosis, and considered that the lobulation was due to a coarse fibrosis induced by the toxines of tuberculosis.

ALTERATION IN THE RELATIVE SIZE OF THE RIGHT AND LEFT LOBES.

Occasionally the normal size of the right or of the left lobe is altered with a corresponding change in the relative and absolute size of the other lobe.

In rare instances the liver, though in its normal position, shows the lobulation seen in transposition of the viscera, the right lobe being small and the left large; or transposition of the lobes without *situs transversus*.

J. Davy [‡] gives a description of a case in which the left lobe was twice the size of the right.

---

[*] Moser: Medical Record, May 7, 1898, p. 671.

[†] Hanot: Gaz. des Hôp., 1893, p. 902.

[‡] Davy, J.: Diseases of the Army, p. 427.

In some instances there is no manifest cause for this reversal of the normal lobulation of the liver, and it may be supposed that it depends on some alteration of the circulation in fœtal or early life. In other instances the diminution in size of the right lobe is manifestly due to syphilitic changes leading to cicatricial contraction.

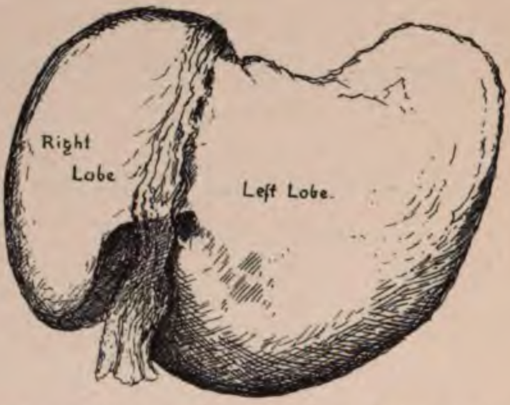

FIG. 1.—LIVER WITH LARGE LEFT LOBE AND SMALL RIGHT LOBE; THE GALL-BLADDER WAS ON THE RIGHT LOBE. (Drawn by Dr. G. H. Goldsmith.)

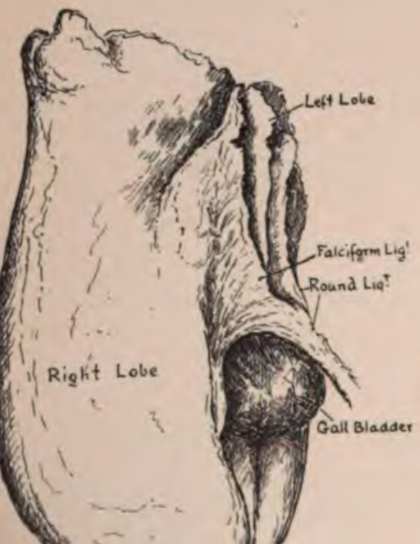

FIG. 2.—SHOWS EXTREME DWARFING OF THE LEFT LOBE OF THE LIVER. (Drawn by Dr. G. H. Goldsmith.)

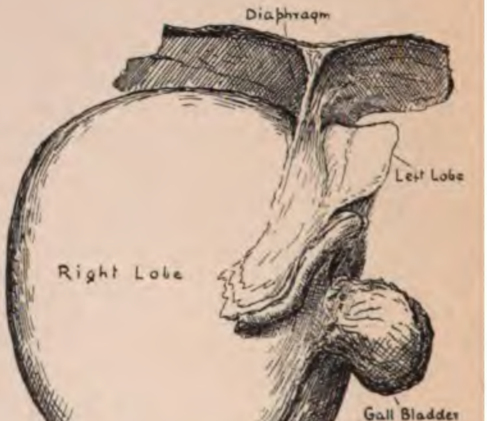

FIG. 3.—SHOWS DWARFING OF LEFT LOBE. GALL-BLADDER PROJECTS FROM THE LEFT MARGIN OF THE LIVER AND HAS ITS LONG AXIS IN THE TRANSVERSE AXIS OF THE BODY. (Drawn by Dr. G. H. Goldsmith.)

Penrose * records this in acquired syphilis and Lazarus-Barlow † in tardive congenital syphilis.

Dwarfing of the left lobe is occasionally seen; it may be merely represented by a little flap of hepatic tissue. In these cases the left lateral ligament is correspondingly small and the falciform ligament arises from the left margin of the liver. The stomach is thus abnormally exposed, and the whole of the gall-bladder is visible from the front and projects from the left lateral margin of the liver. Owing to the disturbed relation of the lobes the gall-bladder may be so displaced as to lie with its long axis in the transverse axis of the body. (*Vide* Fig. 3.)

There is seldom any very manifest reason why the left lobe should be so atrophied, and it may again be suggested that it is due to some disturbance of the circulation in fœtal or in early life. The change may be associated with other congenital defects.

In a case reported by Garrod ‡ extreme dwarfing of the left lobe was associated with lobulation of the right lobe of the liver and the presence of two instead of three aortic valves.

In other instances atrophy of the left lobe may be due to syphilis or to other pathological changes taking place later in life.

I have seen atrophy of the left lobe in a case where a large intra-hepatic calculus pressed upon the vessels entering the left lobe of the liver.

MINUTE ACCESSORY LOBES.

Small projections of liver substance—about the size of the terminal phalanx of the forefinger—which in miniature imitate the caudate lobe, are quite common and of no importance or pathological significance. Their usual situation is the under surface of the right lobe, near the portal and longitudinal fissures. When markedly pedunculated, they may form "accessory livers." The Spigelian lobe is sometimes curiously pedunculated.

There is a cast in the Anatomical Museum at Cambridge of a pedunculated lobe attached to the left border of the left lobe; the pedicle is composed of hepatic tissue. Lawrence and Nabarro § described an abnormal process from the left lobe of the liver in association with absence of the inferior vena cava in a female child aged fourteen weeks.

Accessory Livers.—Isolated fragments of hepatic tissue or "rests" have been found in the suspensory ligament; but it is noteworthy that they are very rarely seen. This contrasts with the frequency of accessory suprarenal bodies and of splenunculi.

Pepere ‖ has recently described a remarkable case in which there were innumerable small nodules of hepatic tissue or accessory livers scattered over the peritoneum and great omentum. One with a diameter of 7 cm. formed a solitary adenoma in the liver. Thirty-one years previously Wagner ** described a number of nodules

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[*] Penrose: Trans. Path. Soc., vol. xl, p. 133.

[†] Lazarus-Barlow: Trans. Path. Soc., vol. l, p. 158.

[‡] Garrod, A. E.: Ibid.. vol. xlviii, p. 42.

[§] Lawrence and Nabarro: Journ. of Anatomy and Physiology, vol. xxxvi, p. 63.

[‖] Pepere: Archiv per le Sc. Med., 1902, vol. xxvi, p. 117.

[**] Wagner: Archiv der Heilkunde, 1861.

composed of liver cells in the falciform ligaments of two infants aged nine days and two months respectively.

Chaillous [*] has described a large accessory lobe attached to the anterior border of the liver, to the right of and close to the falciform ligament, on a level with the quadrate lobe; it was pear-shaped, like the gall-bladder. It was found in the body of an infant.

Davy,[†] in the examination of a man aged twenty-three, dead of dysentery, found a small mass about the size of a hazelnut, the structure of which appeared to be the same as that of the liver, attached to the concave surface of that organ by a delicate pedicle.

Mahomet [‡] described an accessory liver attached to the tip of the gall-bladder in a case of cirrhosis; the accessory liver was also cirrhotic. I have seen a somewhat similar condition in a lardaceous liver.

Accessory livers may also be produced by atrophy of the liver cells in the pedicles of the minute accessory lobes so commonly seen on the under surface of the liver, with the result that a small peritoneal ligament unites the accessory liver to the main organ.

It seems possible that some detached lobes seen in adult life may be due to the effects of pressure or to atrophy of some of the liver tissue from interference with the blood-supply. Constriction lobes attached to the lower extremity of the right or more rarely the left lobe are described under the deformities of the liver due to tight lacing. (*Vide* p. 8.) The following may be regarded as examples of atrophy of the intervening liver tissue inducing the appearances of an accessory lobe.

In a specimen in St. George's Hospital Museum the part of the liver representing the left lobe is completely separated for a distance of 3 inches from the rest of the liver; it was also attached by a kind of mesentery to the cardiac end of the stomach.[§]

In a man aged twenty-four there was a vestige only of the left lobe, which was not continuous with the right lobe. (Davy.[‖])

Atrophy may involve the base of attachment of the Spigelian or possibly of the caudate lobe and so lead to a pedunculated lobe. Davy[**] described a pedunculated Spigelian lobe.

It may be mentioned that between the peritoneal layers of the left lateral ligament the remains of a rudimentary lobe can be seen in the presence of hepatic and portal vessels, though the liver cells have disappeared.

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[*] Chaillous: Bull. de la Soc. Anat., Paris, 1898, p. 572.

[†] Davy, J.: Diseases of the Army, 1862, p. 428.

[‡] Mahomet: Trans. Path. Soc., vol. xxviii, p. 147.

[§] Series ix, 161A. See also Dickinson, W. H.: Trans. Path. Soc., London, vol. xvi, p. 160.

[‖] Davy, J.: loc. cit.

[**] Davy, J.: Diseases of the Army, p. 427.

SOME POSTMORTEM APPEARANCES OF THE LIVER.

A few words may be said about certain common though striking postmortem appearances of the liver, which will not be described elsewhere in this work.

POSTMORTEM DISCOLORATION.

The surface of the liver where it has been in contact with the stomach or colon very commonly shows dark purple stains. These stains, which are produced after death and are quite superficial, are due to the action of gases, among them sulphuretted hydrogen, which diffuse through from the colon and stomach and meet with iron in the liver; as a result, some compound like sulphide of iron is manufactured.

Irregular white areas on the surface of the liver are seen in cases of fevers and other infections, and show congestion and degenerative changes. This appearance was formerly thought to be merely due to mechanical pressure exerted after death in laying out the body.

CLOUDY SWELLING.

This is a very frequent, if not the commonest, change seen in the liver in routine postmortem work. The liver is enlarged, heavier than normal, and looks as if it had been boiled, and has a duller, more opaque, and paler aspect than normal. These changes are due to cloudy swelling or parenchymatous inflammation of the liver cells set up by the toxines of numerous diseases. The changes which are shared by other organs, such as the kidneys and myocardium, are especially well seen in pneumonia. In this disease the enlargement of the liver is very considerable. Long ago Bright * thought that the pneumonic lung materially depressed the liver, but it is clear that any increased hepatic dullness below the costal arch is mainly due to cloudy swelling and congestion.

FOAMING LIVER.

Synonym: Emphysematous Liver.

The formation of gaseous cysts in the internal organs has long been recognized and was formerly put down to putrefaction. This change was shown by Welch and Nuttall,† in 1892, to be due to a micro-organism —the Bacillus aërogenes capsulatus. The infection with this microorganism is generally a secondary and terminal event; in other words, this bacillus follows in the wake of other pathogenic bacteria and does not appear till the patient is moribund. To these general rules there are exceptions. Pure cultures of the Bacillus aërogenes capsulatus have been obtained by Pratt and Fulton,* and by Pakes and Bryant;† while from a case of infective endocarditis Gwyn‡ repeatedly isolated the micro-organism from the blood during life.

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* Bright, R.: Abdominal Tumors, p. 255. New Sydenham Society.

† Welch and Nuttall: Bull. Johns Hopkins Hosp., 1892, vol. iii, p. 81.

The micro-organism may be present and yet not give rise to any formation of gas; this was shown in the cases recorded by Gwyn and by Pratt and Fulton. Though this infection may occur in the body during life, there is no evidence that it ever produces gas until death has occurred. The micro-organism may give rise to necrosis of the cells of the liver and to purulent inflammation, as was shown in Pratt's and Fulton's case of cholangitis with multiple abscesses in the liver.

The Bacillus aërogenes capsulatus is anaërobic, and must be distinguished from the bacillus of malignant œdema. It stains with Gram's method. It is very frequently present in the alimentary canal, and has been found to be widely distributed in nature.

Besides the Bacillus aërogenes capsulatus, other gas-producing bacteria must be taken into account; thus, the colon bacillus (Kanthack, Pakes and Bryant) and other members of the aërogenes group, such as the Bacillus mucosus capsulatus (W. T. Howard, Jr.§), have been described as giving rise to gaseous cysts. Welch, however, is rather sceptical about their claim to be regarded in this light.

The liver is the organ most frequently affected. In 23 cases tabulated by Pakes and Bryant, this organ was affected in 15.

Etiology.—As the formation of gaseous cysts is a death agony or postmortem phenomenon, the Bacillus aërogenes capsulatus is often found in association with other micro-organisms. Other micro-organisms probably favour the development of the Bacillus aërogenes capsulatus by diminishing the bactericidal power of the blood, and also by reducing the resistance of parts of the liver. My friend, Dr. J. H. Drysdale, has communicated to me his unpublished results, which show that hot weather is a factor in the production of foaming liver, but that this condition may occur in the absence of any of the ordinary signs of decomposition. It is found much more frequently when there has been recent loss of blood, which seems to favour the entrance of the micro-organisms into the blood or their development in it. Ulceration and injury of the intestines also favour the entrance of the micro-organisms, which are commonly present in the alimentary canal, into the tissues of the body. Incubation of livers, taken at random from the postmortem room, did not give rise to the formation of gaseous cysts, but incubation of livers from cases of hæmorrhage gave positive results showing that the micro-organisms had got into the organs.

It is generally recognized that the infection of the liver may take place either by the blood-stream or by the bile-ducts. Infection most commonly arrives by the portal vein, and is due to some lesion, such as ulceration, in the intestinal tract. The inlet of infection may be in other situations, such as the uterus or the urethra. Direct infection of the bile-duct and gall-bladder from the intestine may occur. In such instances the bile-ducts and gall-bladder may contain gas either in their lumen or in the substance of their walls, especially in the submucous coat. Welch* has met with five cases of interstitial emphysema of the bile-duct or gall-bladder.

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* Pratt and Fulton: Boston Med. and Surgical Journ., June 7, 1900, p. 599.

† Pakes and Bryant: Guy's Hosp. Reports, vol. liv.

‡ Gwyn: Bull. Johns Hopkins Hosp., 1899, vol. x, p. 134.

§ W. T. Howard, Jr.: Journ. of Experiment Med., Oct. 25, 1900, p. 139.

Although the gas-producing micro-organisms may give rise to a septicæmia and be isolated from the blood, it is doubtful whether formation of gas occurs in the living tissues. It may occur very rapidly after death, or, as shown in emphysematous gangrene, in a part of the body that has lost its vitality. On reviewing the whole subject Welch is inclined to the view that gas is formed in the viscera before death. Clinically it has been thought that tympanites may be due to the formation of gas before death.

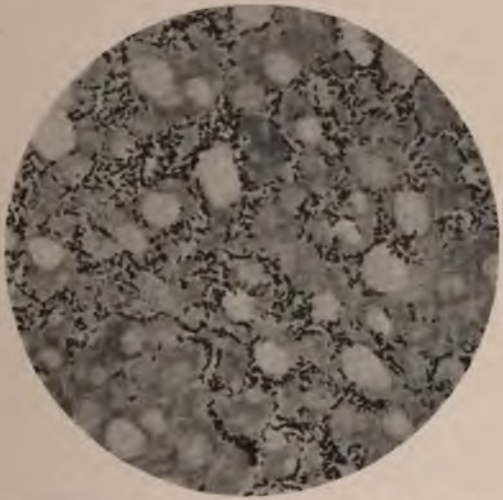

FIG. 1.—PHOTOMICROGRAPH OF A FOAMING LIVER, SHOWING MINUTE GASEOUS SPACES LINED BY THE BACILLUS AËROGENES CAPSULATUS. × 1000. (By Dr. H. Spitta.)

The liver is in a spongy condition from the presence of a number of small gas-containing cysts of various sizes, but mostly small. The organ is usually of a somewhat grayish colour from its inflated condition, which must not be mistaken for multiple cystic disease. The condition may also be met with in other organs—the kidneys, brain, spleen, intestines, pancreas. Some recorded cases of widespread cystic change in the organs of the body may have been of this nature.

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* For a full résumé of the entire subject the reader should refer to Welch's Shattuck Lecture for 1900, Philadelphia Medical Journ., Aug. 4, 1900, p. 202.

ACQUIRED DEFORMITIES.

TIGHT-LACED LIVER.

Synonym: Corset Liver.

Modifications in the shape of the liver due to tight lacing, corsets, and belts are of course common in women, but considerable deformity may be produced in men by the pressure of a tight belt or strap. The effect of tight lacing on the liver varies to a certain extent with fashion, or, in other words, with the position of the waist. Following Hertz,* who has studied the changes produced by tight lacing in great detail, the deformities of the liver may be divided into two main types, though mixed or transitional forms may occur.

I. The liver is flattened and elongated from above downwards so that the upper or diaphragmatic surface is diminished while the anterior is increased. From its larger size the right lobe naturally shows the change more than the left. The liver thus forms a flap which covers the abdominal viscera, though occasionally coils of intestine may pass in front of it. Where the elongated right lobe passes over the right kidney there are atrophy of the hepatic substance and thickening of the capsule, which is opaque and forms a hinge-like ligament between the main part of the right lobe above and the constricted lower portion. This lobe is variously termed partial hepatoptosis, constriction lobe, or the sustentacular formation of the right lobe (Hertz). The constriction furrow is produced by the pressure of the corset in front and the resistance of the kidney behind. The constriction lobe tapers to a point so that the shape of the liver, as seen from the front, is that of a right-angled triangle with the apex downwards. This lobe is often associated with an unduly movable or floating kidney. (Keith.†)

Clinically there is a close resemblance between these constriction lobes of the right lobe and the tongue-shaped or Riedel's lobe, originally described as occurring in special association with gall-stones. The left lobe is prolonged downwards in the same manner, though to a less marked degree, and may even have a constriction lobe attached to it. It has been thought that in the latter event the symptoms were much more marked than in cases where the ordinary tongue-like lobes from the right lobe were present. A tongue-like lobe arising from the left lobe of the liver would tend to exert pressure on the pylorus, duodenum, pancreas, and nerve plexuses which are supported behind by the spine, while on the right side no important viscera or structures would suffer, though the lobe would probably be in contact with the right kidney.

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* Hertz, P.: Abnormitäten in der Lage und Form der Bauchorgane bei dem erwachsenen Weibe, Berlin, 1894.

† Keith, A.: Lancet, 1903, vol. i, p. 711.

From impaired nutrition and diminished resistance the constriction lobe may be more markedly affected by morbid changes than the rest of the liver, or may even be the only part affected. Thus, fibrosis or gummatous change may be confined to a constriction lobe, or secondary new growth may be wholly or chiefly limited to the pendulous lobe.

In a case of carcinoma of the mamma in a woman who died of diabetes the constriction lobe contained large masses of secondary growth, while in the remainder of the liver there were only two small nodules. Frerichs* figures a similar case

On the other hand, the interference with the blood-supply may to some extent protect the constriction lobe against infection by the blood-stream.

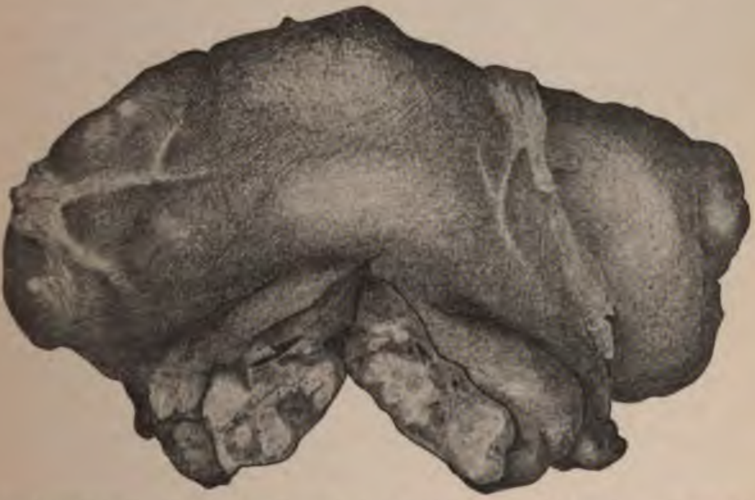

Fig. 5.—Constriction Lobe Attached to the Right Lobe of the Liver, Divided, and its Halves Separated so as to Display Large Secondary Carcinomatous Nodules in its Substance. From case described in the text. (Drawn by L. Jones, M.B., F.R.C.S.)

In 1890 I examined after death the body of a man who died with carcinoma of the pylorus; the liver weighed nine pounds and, except the constriction lobe, attached to the right lobe, was full of secondary new growths.

The whole of the liver, constriction lobe included, may be uniformly affected by cirrhosis.

II. In the second variety of tight-laced liver the organ is displaced upwards as a whole and lies high up in the abdominal cavity. It is thicker above than below, and is curved and moulded over the spine so that the left lobe may touch or even overlap the spleen. Frerichs † figures such a case in which the left lobe of the liver and the spleen were firmly united to each other. The fossa for the inferior vena cava is exaggerated and deepened, while as the result of pressure the right kidney is displaced downwards and its lower end tilted forwards. The lower margin of the right lobe being compressed by the corset or belt, is atrophied in the transverse direction, and shows opacity and thickening of the capsule from local perihepatitis. A triangular constriction lobe may be found attached to the right lobe, but is not such a constant feature as in the previous form, and is never present in connexion with the left lobe. Besides being met with in women, this change in the liver may be met with in men who wear a tight belt.

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* Frerichs: Diseases of the Liver, vol. ii, p. 326. Translation in New Sydenham Society's Library.

† Frerichs: Diseases of the Liver, vol. i, p. 41. Transl. New Sydenham Soc.

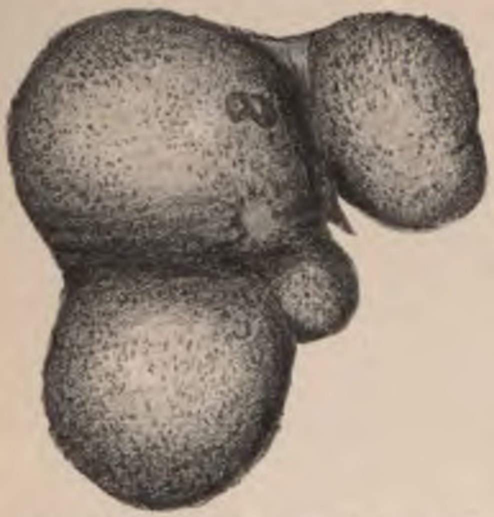

Fig. 6.—Tight-laced Liver Uniformly Cirrhotic.

There are two small cysts on the right lobe. From a woman forty-four years old who died with grave anæmia. The liver weighed forty-one ounces. (Drawn by P. L. Mummery, M.B., F.R.C.S.)

Diaphragmatic Sulci.—When extreme, tight lacing or the pressure of a belt may exercise so much circumferential pressure in an upward direction as to throw the convex surface of the liver into folds. The curve of the convexity is increased, and a number of furrows appear on the upper surface of the right lobe and in rare instances on the left lobe; there may be as many as six of these furrows. They run anteroposteriorly and are deeper posteriorly. When due to the pressure of a belt, a transverse band of thickening of the liver capsule will be found near the anterior inferior margin of the liver.* These furrows have been called "diaphragmatic furrows" by Zahn,† who explains them as the impress left by hypertrophied bundles of the diaphragm and not due to pressure. The change in the diaphragm is due to chronic diseases of the respiratory system, with which these furrows are said to be frequently associated. In 58 cases from the Salpêtrière showing these furrows there were only 5 in which the lungs were healthy. (Séglas.‡)

It is improbable that they are due to pressure exerted by the ribs, inasmuch as the sulci do not correspond to the position of the ribs.

Bagaloglu § has described a single deep furrow on the upper surface of the liver which had no relation to either the ribs or the diaphragm and was not the result of cicatrization. He regarded it as directly due to the pressure of the corset.

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* Weber, F. P.: Trans. Path. Soc., vol. xlviii, p. 113; vol. li, p. 236.

† Zahn: Rev. Méd. de la Suisse Romande, 1882, p. 19.

‡ Séglas: Bull. Soc. Anat., Paris, 1886, p. 163.

§ Bagaloglu: Ibid., Paris, 1899, p. 67.

Furrows of this kind seen in fœtuses, and possibly due to pressure *in utero*, must be distinguished from those due to hereditary syphilis. My own opinion is that these diaphragmatic sulci are chiefly due to pressure.

Cirrhosis may supervene in a liver the subject of tight lacing, and give rise to a uniform change. (*Vide* Fig. 6.) Local changes probably due to chronic venous engorgement, and resulting in fibrosis, may occur in the portion of the liver below the tight-lacing constriction.

Clinical Features.—Tight-laced livers are often associated with dyspepsia, which may be partly due to the abdominal or gastric embarrassment produced by a tight corset. In other cases the symptoms are due to visceroptosis, which is often associated with tight lacing. Keith* has insisted on the importance of tight lacing as a cause of gall-stones, and symptoms of cholelithiasis are not uncommon in patients who have tight-laced livers. But in a very considerable proportion of patients with livers deformed by tight lacing no symptoms referable to that organ are present. A point of considerable interest about tight-laced or corset livers is that the constriction lobe may, when accidentally detected, be easily mistaken for something more important, such as a floating kidney, a tumor of the pylorus or transverse colon, a dilated gall-bladder, cysts of the pancreas or of the mesentery, or in extreme cases for a fibromyoma of the uterus, an ovarian tumor, or appendicitis. The connecting bridge between the constriction lobe and the main part of the liver, as has already been pointed out, is sometimes very thin, and may therefore give a resonant note on percussion, and its actual continuity with the remainder of the organ is therefore difficult to make out.

Treatment.—As a rule, no active treatment for the constriction lobe is either required or justifiable; tight lacing should as far as possible be prevented, but the practitioner requires considerable tact to effect this reform. A straight-fronted corset should be substituted for one which tends to constrict the waist and depress the liver. A properly adjusted belt should be fitted in cases where there is definite enteroptosis with symptoms due to this cause. Dyspeptic and other associated symptoms should be carefully attended to and constipation prevented. In cases where the constriction lobe is the seat of much pain it has been removed, but this can seldom be really necessary. In such cases Bötticher † considers that hepatopexy, or fixation of the constriction lobe, is a more satisfactory method of surgical treatment.

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* Keith, A.: Lancet, 1903, vol. i, p. 639.

† Bötticher: Deutsche Zeitschrift f. Chirurg., July, 1900, vol. lvi.

TONGUE-LIKE LOBES.

Synonyms: Linguiform Lobe, Riedel's Lobe, Partial Hepatoptosis, Floating or Appendicular Lobe.

Although the term partial hepatoptosis has been employed, this condition is quite distinct from complete hepatoptosis or wandering liver, as there is no dropping of the organ as a whole. No doubt confusion between the two conditions has occurred; Glénard considers that the reputed greater incidence of wandering liver in women depends on the fact that some observers have erroneously described tongue-like lobes as wandering livers. These lobes, which are often spoken of as Riedel's, are really much the same as the constriction lobes just described (*vide* p. 8) in the account of the corset liver. It has been thought, especially by Riedel,* that the tongue-shaped lobes are dependent on disease of the gall-bladder, such as inflammation, gall-stones, distention, traction exerted by pericholecystic adhesions. But this explanation does not apply to all the cases.

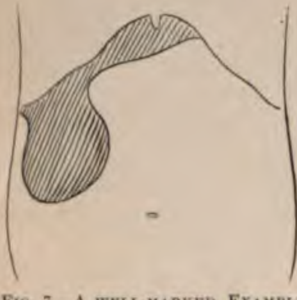

FIG. 7.—A WELL-MARKED EXAMPLE OF RIEDEL'S TONGUE-LIKE LOBE. (After Dr. T. Fisher.)

It is possible that some of the cases of downward projection of the right lobe are connected with or depend on a congenital anatomical variation. This suggestion applies forcibly to cases where this formation is found in babies or young children. As pointed out by Fisher,† there is a considerable amount of variability in the outline of the right lobe, and exaggeration of this might occur as an occasional abnormality without any determining irritation or traction on the part of the underlying gall-bladder. Possibly the formation of Riedel's lobe in some cases of cholelithiasis and its absence in other cases depend on degrees of variability in the outline of the right lobe of the liver.

Dr. Fisher has kindly sent me a drawing of a potential Riedel's lobe in a woman aged twenty-five whose gall-bladder was normal; and I find that six years ago I observed a similar abnormal lobulation in the body of a man aged fifty-eight. If gall-bladder disease arises in such cases, a Riedel's lobe would probably develop much more readily and rapidly than in a normal liver. McPhedran ‡ described seven cases, and regarded the tongue-like lobes as developmental and not artificial. One of his cases was in a baby of eleven months.

Tight lacing must also be taken into account, especially as by displacing the fundus of the gall-bladder downwards it may lead to kinking and occlusion of the cystic duct and so to obstruction to the outflow of the contents of the gall-bladder—a state of affairs which favours catarrhal inflammation and the production of gall-stones. (Keith.§)

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* Riedel: Berlin. klin. Wochen., 1888.

† Fisher, T.: Bristol Medico-Chirurg. Journ., Sept., 1901.

‡ McPhedran: Canadian Practitioner, June, 1896.

§ Keith, A.: The Anatomy of Glénard's Disease. The London Hospital Gaz., Oct., 1902, p. 55.

Incidence.—Tongue-shaped lobes are much more frequent in women. This depends on their causation, both tight lacing and cholelithiasis being much commoner in that sex.

Anatomy.—The tongue-shaped lobes may either taper off gradually into an elongated, thick process from the right lobe, or the connecting pedicle may be reduced to two layers of somewhat thickened peritoneum. In the latter case the tongue-like lobe is freely movable, and during life may appear to be quite distinct from the liver. The gall-bladder may, but need not, be situated on the under surface of the tongue-like lobe, as in two cases excised during life (Martin, Bastianelli); the cystic duct will then run across the pedicle. As a rule, the tongue-like lobe is not perfectly normal in structure; from repeated attacks of congestion it may show fibrosis, and degeneration, atrophy, and pigmentation of the liver cells, and hæmorrhages. It has been found to be affected with gummata when the remainder of the liver was healthy, and may be the seat of secondary new-growth. (Compare p. 9.)

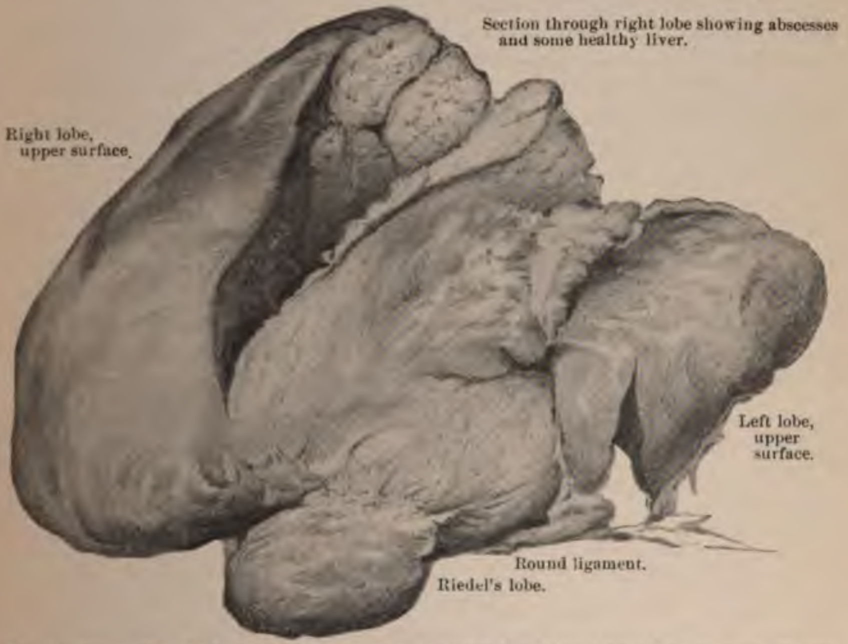
Section through right lobe showing abscesses and some healthy liver.
Right lobe, upper surface.
Left lobe, upper surface.
Round ligament.
Riedel's lobe.

FIG. 8.—SHOWS THE LIVER WITH RIEDEL'S TONGUE-LIKE LOBE AND AREAS OF SUPPURATION DUE TO SUPPURATIVE CHOLANGITIS.

From a case of cholecysto-colic fistula due to gall-stones. (Drawn by Dr. E. A. Wilson.)

Roux* has described primary carcinoma starting in a tongue-like lobe. In his case there was calculous cholecystitis. In similar cases care must be taken to see that the growth does not start in what is a much commoner situation, viz., the walls of the gall-bladder.

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* Roux: Rev. Méd. de la Suisse Romande, Feb. 20, 1897.

Physical Signs.—There is a movable abdominal tumor on the right side of the abdomen, which descends with the diaphragm and the liver on respiration. It is dull on percussion, but this is seldom continuous with the liver dulness, as there is usually a band of resonance between it and the liver. It may be distinctly tender on pressure. It may descend as low as the right iliac region and give rise to difficulty in diagnosis from appendicitis, etc.

Symptoms.—The existence of a tongue-like lobe may be discovered accidentally and may not be accompanied by any bad effects. Usually the symptoms associated with the existence of a tongue-like lobe are due to calculous cholecystitis, which may have played an important part in the production of the deformity. The patient may have been conscious for some time of enlargement and alteration in shape of the abdomen and of a slowly growing tumor, as in Martin's case, where a tumor had existed for twelve years. There are often a feeling of oppression and heaviness in the right hypochondrium and pain in the back. Abdominal pain may be paroxysmal, like gall-stone colic, or may be constant; the pain is usually relieved by rest in the recumbent position. Intense venous engorgement of the lobe may give rise to attacks of palpitation, vomiting, and collapse. Jaundice and ascites are rare and are due to some definite cause, such as gall-stones or chronic peritonitis.

Diagnosis.—Riedel's lobe may appear to have no definite connexion with the liver, and thus appears as a movable abdominal tumor and may easily be mistaken for a floating kidney. An instructive case in point is recorded by C. Martin.*

A woman aged thirty-six had had a lump in her abdomen for twelve years which had recently grown rapidly and become tender and painful. An oval tumor about the size of a six months' pregnancy filled the right half of the abdomen; it was tense and very mobile, dull on percussion, and separated from the liver by a band of resonance. It was thought to be an unusually mobile kidney. Laparotomy revealed a pedunculated accessory lobe of the liver bearing the gall-bladder; it was successfully removed. Its weight was 3¾ pounds.

Bastianelli † describes a case in which a displaced cancerous kidney was diagnosed; laparotomy revealed a floating lobe of liver, with the gall-bladder on its under surface. This piece, weighing 500 grammes (18.75 ounces), was successfully removed; on section there were gummata in it, but not in the remainder of the liver.

A tongue-like lobe may be thought to be some other form of abdominal tumor, such as a solid growth in the omentum, a tumor of the pylorus, a distended gall-bladder, or a cyst of the pancreas or mesentery, or in extreme cases a fibromyoma of the uterus, ovarian cyst, or appendicitis.

In a case under my care in St. George's Hospital the gall-bladder was greatly thickened, probably from calculous cholecystitis, was adherent to the colon, and accompanied by a well-marked tongue-like lobe which before laparotomy was thought by some to be a floating kidney or a growth in the transverse colon.

Treatment.—In cases where a tongue-like lobe is diagnosed, treatment is only necessary when pain or discomfort is present. If there is any underlying cholecystitis or cholelithiasis, treatment should be directed to those conditions. In seven cases where the morbid condition of the gall-bladder was treated the tongue-like lobe disappeared (Terrier and Auvray[*]). An ill-fitting corset or one which presses on the liver should be replaced by a straight-fronted corset, and tight lacing or constriction of the waist by a belt should be prevented. It is not often that radical treatment, such as stitching the lobe to the abdominal parietes or its complete removal, is necessary.

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* C. Martin: Birmingham Med. Rev., Feb., 1898, p. 92.

† Bastianelli: Il Policlinico, April, 1895. Epitome, Brit. Med. Journ., May 4, 1895.

In three cases the tongue-like lobe has been stitched to the abdominal parietes with success (Billroth,[†] Tscherning,[‡] Langenbuch[§]). Removal of the lobe has been carried out by Bastianelli, Martin, and Lockwood.[‖]

Effect of Tight Lacing on the Gall-bladder.—The gall-bladder is frequently dilated. Hertz[**] found it so in 24 out of 41 cases. The downward displacement of the duodenum brings tension to bear on the cystic duct, which even under normal conditions requires a spiral valve to keep it open (Keith[††]), and thus leads to obstruction. The resulting retention of bile and mucus in the gall-bladder may tend to elongation of the right lobe, and so give rise to, or accentuate, the tongue-like lobe seen in many corset livers. Retention of bile in the gall-bladder disposes to cholecystitis and cholelithiasis, and the predominance of female sufferers from gall-stones is no doubt in part due to the bad effects of the corset.

When calculi are present in the gall-bladder, the pressure exerted by the corset may, as suggested by Fütterer,[‡‡] increase the friction between the gall-stones and the mucous membrane of the gall-bladder, and thus help to explain the greater frequency of primary carcinoma of the gall-bladder in women. In this connexion it is noteworthy that the larger bile-ducts, which are not affected in the same way by corsets or belts, are more often the site of primary carcinoma in man.

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[*] Terrier et Auvray: Rev. de Chirurg., 1897.
[†] Billroth: Wiener med. Wochen., 1886, No. 14.
[‡] Tscherning: Centralblatt f. Chirurg., 1888, p. 426.
[§] Langenbuch: Deutsche med. Wochen., 1888.
[‖] Lockwood, C. B.: Lancet, 1903, vol. ii, p. 223.
[**] Hertz: Abnormitäten in der Lage und Form der Bauchorgane, 1894.
[††] Keith, A.: Lancet, 1903, vol. i, p 639.
[‡‡] Fütterer, G.: Chicago Medical Society, April 1, 1897

DISPLACED LIVER.

SYNOPSIS OF THE FORMS OF MALPOSITION.

CONGENITAL.

- Transposition.
- Ectopia.
- In diaphragmatic hernia.

ACQUIRED.

- In diaphragmatic hernia.
- In spinal curvature and in rickets.
- In tight lacing.

Thoracic conditions displacing the liver.

- Pleural effusion and pneumothorax.
- Malignant disease of lung, etc.
- Pericardial effusion.

Abdominal conditions displacing the liver.

- Downwards.
- Forwards.
- Backwards.
- Laterally.

Apart from enlargement due to tumors or other causes, the liver may occupy an abnormal position under numerous and very various conditions. A displaced liver which is at the same time freely movable is a wandering liver, and is dealt with under that heading (*vide* p. 22). Here we are only concerned with displaced livers which are not more movable than normal. Malposition may conveniently be divided in the first instance into (*a*) those of congenital origin and (*b*) those acquired in later life; the latter class is by far the larger.

CONGENITAL MALPOSITIONS.

Transposition.—In complete transposition of the viscera the liver will be on the left side, but occasionally the heart may be congenitally transposed without the liver sharing in the change. Transposition of the liver without the other viscera being affected is very rare indeed.

Complete transposition of the viscera may lead to an erroneous diagnosis if the condition is not recognized. In a case, recorded by Billings,* of cholelithiasis in a patient with *situs transversus* a physician had diagnosed acute yellow atrophy from absence of the hepatic dulness on the right side.

Congenital Ectopia of the Liver.—(Synonyms: *Hepatomphalos, Hepatocele.*)—From congenital defect of the muscles of the abdominal wall the liver may project under the skin either at the umbilicus or in the middle line between the umbilicus and the ensiform cartilage. Congenital hernia or ectopia of the organ at the umbilicus has been called hepatomphalos. The tumor is firm, dull on percussion unless coils of intestine are also present in the sac, and is continuous with the liver dulness. It may be easily reduced, but reappears on removal of the pressure. On the other hand, the liver may become adherent to the walls of the umbilical sac and thus be irreducible. This was the case in a baby aged three weeks.[*] Bullard[†] met with a case where the liver was described as being herniated into the umbilical cord.

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* Billings: Philadelphia Med. Journ., 1900, p. 670.

Displacement of the Liver as the Result of Congenital Diaphragmatic Hernia.—Congenital defects of the diaphragm may give rise either to a free communication between the peritoneal and pleural cavities or, from deficiency of the muscular tissue of the diaphragm only, to a membranous pouch which projects up into the thorax. Congenital deficiency of the diaphragm is commoner on the left side (Jaffé[‡]) and may allow the left lobe of the liver to enter freely into the thorax.

In a case of Porak and Durante's[§] the peritoneum communicated freely with the left pleura, and the left lobe of the liver was found behind the sternum.

ACQUIRED DISPLACEMENTS.

In Diaphragmatic Hernia.—This may occur as part of a severe injury, the diaphragm being torn across and the stomach, colon, spleen, or part of the liver may pass into the thoracic cavity. Diaphragmatic hernia when found in adult life without any history of injury may of course be congenital in origin, and in cases where the herniated viscera have been found enclosed in a sac composed of the attenuated remains of the diaphragm or merely of the opposed pleura and peritoneum, this would appear probable. Pouching due to weakness near the œsophagus or xiphoid cartilage may, however, be an acquired condition. In some cases a rent in the diaphragm may have been due to an injury received years before and almost or quite forgotten. The nature of the defect may then be regarded as congenital, whereas it is really acquired. In a considerable number of cases of diaphragmatic hernia the condition is found to have been preceded by traumatism years before.

Traumatic diaphragmatic hernia is nearly always on the left side, since the support provided by the liver tends to protect the right leaflet from rupture. The liver is much less often displaced into the cavity of the thorax than the stomach, colon, intestines, or spleen.

Blum and Ombrédanne[‖] refer to three cases of traumatic diaphragmatic hernia in which the liver projected into the pleural cavity. In one of these, in which there was a history of a fall fourteen years before, part of a cancerous liver projected into the left pleura. (Dietz's case.)

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[*] J. Hutchinson: Medical Times, 1870, vol. i, p. 397.
[†] Bullard: American Medicine, Nov. 8, 1902.
[‡] Jaffé: Trans. Path. Soc., vol. xlv, p. 224.
[§] Porak et Durante: Bull. Soc. Anat. Paris, 1901, p. 354.
[‖] Blum et Ombrédanne: Archiv. Général de Méd., 1896, vol. i, p. 1, 178.

Part of the liver may pass through the rent and become tightly constricted at the margin of the rent like a strangulated hernia.

The following case, the postmortem examination of which I saw, was recorded by Dr. Ogle in the transactions of the Pathological Society, vol. xlviii, p. 114. A boy, aged sixteen years‘ who had had an accident six years before, was admitted with frequent vomiting and signs of a left pleural effusion; aspiration did not remove any fluid. At the autopsy the cardiac end of the stomach and the left lobe of the liver were found in the left pleural cavity, having passed through a rent in the central tendon of the diaphragm, which had a diameter of 1½ inches. The intrathoracic part of the left lobe was connected by a thin atrophied pedicle with the rest of the liver and formed a lump 5 by 4 inches which looked very like a hard, deeply congested spleen. On section it was deep red in parts with white areas, and was mottled. Microscopically there were much hæmorrhage, a quantity of blood-pigment, and degeneration of the liver cells.

In Spinal Curvature and in Rickets.—The liver though structurally normal may be very considerably displaced by spinal deformity. Its lower edge may be below the umbilicus and the organ may be unduly movable. In rickets the deformity of the chest to some extent depresses the liver, which is usually somewhat enlarged from the action of intestinal poisons. The view that the liver is enlarged in rickets is true, but the increase in the downward extent of the hepatic dulness is often partly due to displacement by thoracic deformity.

Tight Lacing, etc.—The deformities of the liver resulting from tight lacing and artificial constriction of the lower part of the thorax are described elsewhere (p. 8). In these conditions the liver may be displaced upwards as a whole, or even downwards, according to the position of the "waist," but most commonly the right lobe is elongated downwards and has a constricted area, corresponding to the line of pressure, uniting the floating lobe to the main part of the right lobe.

Thoracic Conditions Giving Rise to Displacement of the Liver.—*Effusion into the Right Pleural Cavity.*—A large serous effusion or empyema will effect this, but inasmuch as these conditions are usually relieved by paracentesis, the best examples of displacement of the liver due to disease of the pleura are seen in cases of right pneumothorax. A neglected or latent pleural effusion may, however, reach a large size and then produce marked displacement of the liver.

A man aged forty-three years arrived at the hospital in a state of collapse and died in a few minutes. At the autopsy, which I performed, the right pleura contained 10 pints of pus, the liver was greatly depressed, its lower edge being on a level with the anterior superior spines of the ilia.

Besides being displaced downwards the liver is rotated on its anteroposterior axis. The right leaflet of the diaphragm being depressed or even presenting its convexity downwards, the right lobe is much more depressed than the left, and the left lobe swings upwards, the whole organ being pushed towards the left.

A pneumothorax on the right side may in rare cases lead to acute dislocation of the liver when the intrathoracic pressure is raised, as a result of a valvular communication between the lung and the pleural cavity.

Stiller * records a case where a pneumothorax developed as the result of sneezing in a healthy man and the liver was depressed so as to form a large abdominal tumor.

A pleural effusion or pneumothorax on the left side may give rise, if excessive, to downward displacement of the left lobe of the liver.

Malignant Disease of Lung.—Very extensive malignant disease affecting the lung and greatly increasing its volume may displace the liver downwards.

This displacement was very marked in a boy with an enormous calcifying sarcoma in the thorax, secondary to sarcoma of the thigh, who died in St. George's Hospital under the care of Dr. Penrose in April, 1898. The growth pressed the right leaflet of the diaphragm down so that its under surface was convex, the liver was depressed, and its lower border was on a level with the umbilicus. It was not more freely movable than normal.

In mediastinal growths the liver is not displaced unless, as not infrequently occurs, there is a large pleural effusion at the same time.

In emphysema the downward displacement of the liver is often easily detected, but the increased downward extent of the liver is not extreme unless there is, in addition, chronic venous engorgement due to failure of the right side of the heart.

Pneumonia.—Bright † thought that pneumonia was the direct physical cause of the liver being below the costal arch. But the cloudy swelling of the liver is in part responsible for the projection of the liver downwards. When the whole lung is solid, the diaphragm may be in the position of maximum inspiration, and as a result the liver is somewhat depressed. I have seen downward displacement of the right half of the diaphragm and of the liver at the autopsy of a child with extensive tuberculous pneumonia of the right lung.

Pericardial Effusion.—A large pericardial effusion will depress the diaphragm and with it the liver.

In a case figured by Sibson,‡ where the pericardium contained 3¼ pounds of fluid, the right lobe of the liver was displaced and tilted just in the same manner as in a right-sided pleural effusion.

Abdominal Conditions Leading to Displacement of the Liver.—Generally speaking, abdominal conditions which displace the liver do so in an upward direction, but occasionally the liver may be depressed, while in other cases it may be pushed, drawn, or rotated laterally. Growths arising from the retroperitoneal space may push the liver forwards and, conversely, gas free in the peritoneal cavity or under certain conditions tympanitic distension of the intestines may separate the liver from the anterior abdominal wall.

Abdominal Conditions Displacing the Liver Downwards.—A subdiaphragmatic or subphrenic abscess on the right side may pass between the diaphragm and the convexity of the right lobe and displace the liver downwards. A right-sided subphrenic abscess may be the result of a gastric ulcer situated near the pylorus, of a perforating duodenal ulcer, though the resulting peritonitis unfortunately is rarely localized, and may then contain gas as well as pus, or tract up from perforation of an inflamed appendix, situated in what is not an infrequent abnormal position, viz., running up over the right kidney. Besides these extrinsic origins for a right-sided subphrenic abscess, an abscess in the liver itself, a suppurating hydatid cyst or the multiple abscesses of pylephlebitis may perforate into the potential space between the liver and diaphragm and give rise to a collection of pus there and so to downward displacement of the liver. In these cases the liver is itself enlarged and the condition is almost the same as hepatic abscess.

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* Stiller: Wien. med. Wochen., May 4, 1901.

† Bright, R.: Abdominal Tumours, p. 255, New Sydenham Society.

‡ Sibson: Russell Reynolds' System of Med., vol. iv.

A hydatid cyst projecting from the convexity of the liver rather encroaches on the thorax than pushes the liver downwards. Shattuck[*] described a single cystic adenoma of the bile-ducts containing a gallon of clear fluid which pushed the liver downwards.

As the result of peritoneal adhesions due to local peritonitis, *e. g.*, from appendicitis or inflamed tuberculous glands, as in a case of Sir F. Treves,[†] the liver may be pulled downwards towards the pelvis. A liver which in the first instance was freely movable may subsequently become fixed in an abnormal position by local peritonitis or perihepatitis. Thus Richelot[‡] found the liver fixed in the right iliac fossa close to the cæcum.

Upward Displacement of the Liver.—Ascites, flatulent distension of the intestines, excessive dilatation of the colon, or the presence of large abdominal tumors, such as ovarian cysts, uterine fibromyomata, etc., push the liver and diaphragm up and thereby encroach very seriously on the capacity of the thorax. The convexity of the diaphragm may then be on a level with the third rib or even higher.

As an example of extreme displacement of the liver from the pressure exerted by ovarian cysts reference may be made to a remarkable case recorded by F. A. Baldwin[§] in which there were four ovarian cysts, two large and two small, in the abdomen of a woman aged fifty-nine years. The cysts contained 18 gallons of fluid and were estimated to weigh 185½ pounds. The highest point of the liver was on a level with the upper border of the third rib in the nipple line.

When this upward displacement is very considerable, the liver may largely or even entirely cease to be in contact with the anterior abdominal wall and undergoes a very striking alteration in its relation to other organs. The anterior surface travels backwards and becomes posterior, while the inferior surface looks forwards and upwards instead of downwards and backwards. This is due to the liver moving upwards on a transverse axis running through its connexion with the inferior vena cava, which is relatively a fixed point.

Displacement Forwards.—A retroperitoneal growth or a pancreatic cyst may in rare cases push the liver forwards, a growth of the right suprarenal capsule may displace the right lobe forwards, while a pancreatic cyst will tend to force the left lobe into undue prominence. An aortic aneurysm near the pillars of the diaphragm may so displace the liver forwards as to suggest a new-growth in that organ. In Beatty's * case of aortic aneurysm in this situation the liver appeared steadily to increase in size.

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[*] Shattuck: Boston Med. and Surg. Journ., April 26, 1900.

[†] Treves, F.: Brit. Med. Journ., 1896, vol. i, p. 1.

[‡] Richelot: Gaz. des Hôp. Paris, p. 783.

[§] Baldwin: Brit. Med. Journ., 1900, vol. ii, p. 80.

Displacement Backwards.—Occasionally coils of intestine or the colon may intervene between the liver and the anterior abdominal wall, thus displacing the liver backwards. This occurs in acute yellow atrophy where the great diminution or even complete disappearance of the liver dulness is largely due to the flabby liver allowing resonant bowel to come between it and the abdominal parietes. In cases of perforation free gas in the peritoneum may pass between the liver and the anterior abdominal wall and displace the organ backwards. In rare cases a distended piece of small intestine or colon may get between the anterior surface of the liver and the abdominal wall. This accounts in all probability for the occasional absence of liver dulness seen in cases during life for which no definite cause, such as acute yellow atrophy, a subphrenic pyopneumothorax, or perforation, is forthcoming. In these cases, in which there may be no abdominal symptoms, a thickening of the capsule of the liver corresponding to the abnormally situated piece of intestine may sometimes be found after death.

Dilatation of the stomach or extreme degrees of dilatation of the descending colon will tend to rotate the liver towards the right.

T. Fisher † figures cases of this kind and I have seen several examples of this condition in the postmortem room. In one case the colon lay just anterior to the atrophied bridge of liver substance connecting the constriction lobe with the remainder of a tight-laced liver.

A displaced liver is, as a rule, not more movable than one in its normal position. It differs from a wandering liver in this respect, and also in the fact that it cannot be replaced in its normal position, while, in addition, a definite cause for its displacement is often forthcoming. Symptoms which might be referred to a displaced liver, such as weight, pain, and heaviness, are generally thrown into the shade by those of the condition responsible for the displacement. The various forms of enlargement of the liver, fatty, lardaceous, leukæmia, new-growth, abscess, cirrhosis, etc., must be differentiated from a displaced liver by a careful physical examination of each individual case.

The treatment of a displaced liver is that of the condition giving rise to it.

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* Beatty: Dublin Hosp. Reports, vol. v.

† Fisher, T.: Bristol Medico-chirurg. Journ., Sept., 1901.

HEPATOPTOSIS.

Synonyms: Wandering Liver, Movable Liver, Prolapse or Dislocation of the Liver.

By the term wandering or movable liver is meant one which, being unduly displaceable, leaves its normal position and forms an abdominal tumor.

Historical.—Cantani [*] in 1866 described a clinical case of movable liver, but there was no autopsy. Though Cantani's name is connected with the recognition of its clinical features, the anatomical condition had been described long before.

Heister, as far back as 1754, published the account of an autopsy, with a plate showing the position of the liver. Gunzius (1744), Buchoby (1768), and Sauvage (1768) also referred to cases. Wickham Legg [†] first drew attention to the subject in this country. In recent times Glénard [‡] has done much to direct attention to the subject.

Hepatoptosis is analogous to a wandering spleen. Both these organs are normally "floating" in the abdominal cavity, for while tethered in their normal positions by peritoneal ligaments, they are supported by the mutual pressure of the other abdominal viscera, especially the elastic pad formed by the intestines, and are not fixed and packed round by fat in the way that the kidneys are. The term "floating," which is accurately applied to an unduly movable kidney, is an equally appropriate epithet for a normal liver or spleen, and therefore does not describe an abnormally mobile condition of these viscera. The liver normally moves during respiration, descending with the diaphragm on inspiration half an inch below the costal arch in the right nipple line. A dilated stomach or distension of the colon on the left side will rotate the liver to the right. When this displacement is greatly exaggerated, the state of affairs in wandering liver is imitated.

There is a great difference between an unduly movable liver on the one hand, and one which is merely pushed out of place by a tumor or pleural effusion on the other hand. A displaced liver is not necessarily, or indeed usually, more movable than one in the normal position. Again, the tongue-like and constriction lobes attached to the right lobe of the liver in tight lacing and other conditions must be distinguished from a wandering liver. The wandering liver may be spoken of as total hepatoptosis, while the constriction and tongue-like lobes have been called partial hepatoptosis.

Existence of Total Hepatoptosis.—From the collected cases of Faure, Einhorn, Graham, Bötticher, Glénard, and Telaky, it has been estimated by Dutton Steele[*] that, in all, about 100 cases of undoubted total hepatoptosis are on record, of which 44 have been confirmed by operation or autopsy. Its existence, therefore, admits of no reasonable doubt, but from its intimate attachment to the diaphragm, the liver is not so often affected by visceroptosis as the other abdominal organs.

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[*] Cantani: Annali Universali de Medecina, vol. clxxxxviii, p. 373, 1866.
[†] W. Legg: St. Bartholomew's Hosp. Reports, vol. xiii, p. 141, 1877.
[‡] Glénard: Les ptoses Viscérales, Paris, 1899.

The existence of movable livers has been doubted from time to time, and the clinical signs of the condition have been explained as due to causes such as floating kidneys, renal or other tumors. This was the view taken by Wickham Legg,[†] the first writer (1877) on this subject in this country. In some cases where a floating liver was diagnosed during life the liver has been found in its natural position after death (P. Müller,[‡] Crawfurd).

According to Hertz[§] and Glénard,[‖] some at any rate of the cases described as wandering livers were in reality constriction lobes attached to a thinned and elongated right lobe. The part below the corset furrow may thus be mistaken for the whole liver, especially when it is very mobile and the abdomen is lax and pendulous. Glénard, indeed, considers that the predominance of the female sex in the recorded cases of movable liver is thus explained.

Frequency.—Well-marked examples of hepatoptosis with definite symptoms are rare. Minor degrees, however, are fairly often found when looked for; thus Glénard,[**] from researches on a large number (3500) of invalids suffering from various disturbances of nutrition, estimated that 20 per cent. of these patients present some degree of it. He put the numbers at 25 per cent. for males and 15 per cent. for females, thus reversing the usual incidence of really movable livers in the two sexes. For there can be no doubt that cases with characteristic symptoms are usually met with in women with pendulous abdominal walls who have borne many children. It is noteworthy that Glénard has found some degree of hepatoptosis with greater frequency in his later papers; thus, in 1886, he estimated that it occurred in 2 per cent. and in 1892 in 20 per cent. of patients with diseases of nutrition. It is fairly safe to assume that many of the latter cases, which would escape observation in less practised hands, do not suffer from the effects of the condition.

Sex.—The female sex provides the vast majority of cases of wandering livers. In 80 cases described as hepatoptosis and collected from literature by Glénard,[††] 69 at least were in women. In Graham's[‡‡] 70 cases 56 were in women. Max Einhorn[§§] in private practice noted 21 women and 9 men. As already mentioned, Glénard's own observations, which include minor degrees of hepatoptosis, were to the effect that hepatoptosis is really more frequent in men, its apparently greater incidence in females being explained by cases of partial hepatoptosis (Riedel's lobes, constriction lobes) erroneously regarded as complete hepatoptosis.

Age.—The majority of patients suffering from hepatoptosis are over forty years of age. Treves[*] puts the age at between thirty-five and sixty. In exceptional instances it is met with in children.

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[*] Dutton Steele: University of Penna. Med. Bull., Jan., 1903, p. 424.

[†] Legg: St. Bartholomew's Hosp. Reports, vol. xiii, p. 141, 1877.

[‡] P. Müller: Deutsch. Archiv f. klin. Med., 1874, Bd. xiv, S. 146.

[§] Hertz: Abnormitäten in der Lage und Form der Bauchorgane, 1894.

[‖] Glénard: Les ptoses Viscérales, Paris, 1899.

[**] Glénard: Les ptoses Viscérales, Paris, 1899, p. 503.

[††] Glénard: Les ptoses Viscérales, Paris, 1899, p. 625.

[‡‡] J. E. Graham: Canadian Practitioner, June, 1895.

[§§] Einhorn, Max: Medical Record, Sept. 16, 1899.

Freeman,[†] in 496 autopsies on children, met with four examples of hepatoptosis due to relaxation and elongation of the suspensory ligament; the right lobe came down into the pelvis, the left lobe being the only part of the liver touching the diaphragm, while the upper surface was turned to the right.

Factors Responsible for the Normal Position of the Liver.—As bearing on the causation of hepatoptosis it will be well to refer to the factors which maintain the liver in its normal position. These are: (1) The attachment of the liver by the inferior vena cava to the diaphragm. This, according to Faure,[‡] is the most important agent in retaining the liver in its place, and by itself is capable of sustaining a weight of 27 kilogrammes, as against 20 kilogrammes which the other suspensory ligaments can support. (2) The peritoneal ligaments, the falciform, coronary, and lateral, and the connective tissue uniting the right lobe of the liver to the diaphragm (the mesohepaticon). Graham's[§] observations on the dead body showed that they can support the liver independently of the abdominal walls, and both he and Dutton Steele[‖] found that cutting these ligaments led to a condition which was much the same as that in hepatoptosis. These observations show that in spite of Symington's[**] statement that under ordinary conditions the suspensory ligaments are not tense, they can, when intact and healthy, prevent any abnormal or excessive descent of the liver. (3) The healthy tone of the abdominal muscles which keeps up the intra-abdominal pressure and makes the intestines act as an elastic pad or support for the liver. In the rare cases of congenital absence of the muscles of the abdominal wall the liver has been found to be extremely movable. (Guthrie.[††])

Intra-hepatic blood tension may possibly play a part in keeping the liver in its normal position. Injection of water into the vessels of the liver was found by Glénard and Siraud[‡‡] not only to increase its size, but to straighten out its under or concave surface, which became more convex. It is further stated that in chronic congestion of the liver the organ keeps well in its place even though the abdominal walls are flaccid. Alteration in the intra-hepatic blood-pressure may therefore possibly have something to do with dropping of the liver.

Causation of Hepatoptosis.—An unduly movable liver might depend on some congenital defect or abnormality of the suspensory apparatus, such as an imperfect development of the falciform or coronary ligaments, or upon elongation, which when extreme might justify the term "mesohepar." There is, however, very little anatomical evidence to support this theory. It is quite reasonable to suppose that elongation of the suspensory ligaments may be congenital in the sense that there is an hereditary weakness which, like that underlying hernia and general dropping of the viscera (Glénard's disease), allows elongation of the ligaments to occur later in life under conditions which in ordinary persons would not have this effect. Another equally tenable view is that the tendency to elongation is acquired and depends on degeneration or atrophy of the suspensory ligaments induced by malnutrition and general debility. The associated enteroptosis, pendulous abdominal walls, and lineæ albicantes may be regarded as manifestations of the same process, and, as will be seen later, they favour the production of hepatoptosis. Elongation of the suspensory ligaments must occur in order to allow the liver to become movable.

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[*] Treves, F.: Lancet, 1900, vol. i, p. 1339.

[†] Freeman: Archives of Pediatrics, 1900, p. 81.

[‡] Faure: Thèse, Paris, 1892.

[§] Graham, J. E.: In Loomis and Thompson's System of Practical Med., vol. iii, p. 414.

[‖] Dutton Steele: University of Pennsylvania Med. Bull., vol. xv, p. 424, Jan., 1903.

[**] Symington: Trans. Medico-chirurg. Soc., Edinburgh, vol. vii, p. 53.

[††] Guthrie, L. G.: Trans. Path. Soc., vol. xlvii, p. 139.

[‡‡] Glénard and Siraud: Lyon Médical, June, July, 1895.

In cases where the suspensory ligaments are unduly extensible, dragging on the liver by peritoneal adhesions, tumors, cysts, or large accumulations in the gall-bladder may lead to elongation of the ligaments, and so to an excessively movable and displaced liver. This condition resembles a simple displaced liver (*vide* p. 16), but differs from it in excessive mobility. Total hepatoptosis due to traction is a rare event, and must be distinguished from the elongation of the right lobe (Riedel's lobe, partial hepatoptosis) seen in many cases of cholelithiasis (*vide* p. 12).

Thus in a case of Sir F. Treves,* a young woman aged twenty-two years, the liver descended 2 inches on assuming the erect posture; there was general enteroptosis due to traction exerted by the great omentum, which was firmly adherent to calcified tuberculous glands in the right iliac fossa.

Tight lacing and corsets are probably extremely important in the production of a freely movable liver. The pressure of the corset and the traction exerted by a heavy skirt at the waist tend to displace the abdominal viscera downwards. The suspensory ligaments of the liver, if degenerate, would thus be easily elongated. Further, tight lacing leads to weakness of the abdominal muscles, and so increases the conditions favourable to hepatoptosis.

Landau † and Hertz,‡ however, who have paid considerable attention to the effects of tight lacing, oppose this view.

Failure of the healthy tone of the abdominal muscles, leading to a pendulous condition of the abdomen with a diminution of intra-abdominal pressure, is an important factor in hepatoptosis. A flaccid abdominal wall removes the support provided to the liver by the intestines, and thus throws the weight of the liver onto the suspensory ligaments, which if not sufficiently strong will stretch and elongate. Weakness of the abdominal walls alone is not sufficient to cause hepatoptosis, and, conversely, hepatoptosis may occur when the abdominal walls are healthy.

In 55 cases of hepatoptosis collected by Graham § only 19 were definitely stated to have pendulous abdomens.

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* Treves: Brit. Med. Journ., 1896, vol. i, p. 1.

† Landau: Deutsch. Archiv f. klin. Med., Bd. xiv, 1875. ‡ Hertz: Loc. cit.

§ Graham, J. E.: Loomis and G. Thompson's System of Practical Medicine, vol. iii, p. 414.

The causes which lead to weakening of the abdominal parietes are chiefly those that produce abdominal distension, such as repeated pregnancy, ascites, intra-abdominal tumors, persistent flatulence, and accumulations of fat. In addition, the wearing of stays and want of exercise diminish the healthy tone of the abdominal muscles, while anæmia, debilitating diseases, and neurasthenia have the same effect. This weakening of the abdominal walls is a most important factor in diminishing the intra-abdominal tension. These conditions being more frequently present in women, abdominal tension is much lower among them than among athletic men. In men who lead a sedentary life, such as tailors and cobblers, however, the intra-abdominal pressure may be low. In women it may even be negative. (Bruce Clarke.*)

Glénard † lays stress on "hepatism" as a factor in the production of movable liver. By "hepatism" he means a chronic nutritional change which may be hereditary or acquired, and may be of two kinds, (*a*) cholæmic, (*b*) uricæmic, corresponding to "arthritism" of some French authors, and to Murchison's "lithæmia." (*Vide* p. 39.)

To sum up: The important disposing factors in the production of hepatoptosis are (1) a weak, extensible condition of the suspensory ligaments and (2) a low intra-abdominal tension due to an atonic condition of the abdominal walls. These conditions of impaired nutrition are very prone to go together and to be accompanied by general visceroptosis.

Associated Conditions.—*Visceroptosis.*—Hepatoptosis may be part of general enteroptosis and the most prominent manifestation of that condition, or it may occur in cases where there is no other manifestation of visceroptosis or only a floating kidney. The association of a floating right kidney with hepatoptosis is comparatively frequent.

In 44 cases of hepatoptosis, verified either by laparotomy or autopsy, Dutton Steele ‡ found 9 cases of floating right kidney, or 20.4 per cent. In 330 cases of nephroptosis recognized clinically by Glénard § in women, there were 70 cases of hepatoptosis.

Neurasthenia, etc.—As already mentioned, neurasthenic conditions and general debility with loss of muscular tone may accompany total hepatoptosis and are probably closely related to the low intra-abdominal pressure. Schwerdt, ‖ indeed, regards visceroptosis as primarily dependent on muscular atony of nervous origin.

Exciting Causes.—A wandering liver in the majority of cases develops gradually, so that there is no definite onset. But in a certain proportion of the cases—according to Graham, in 5 per cent.—there is an acute onset of symptoms suggesting sudden dislocation of the organ. This acute onset may in rare instances be due to severe injuries leading to rupture or laceration of the peritoneal suspensory ligaments, such as the passage of a wheel over the body, falls, or blows. In less extreme cases sudden exertion in lifting heavy weights, violent expiratory efforts, such as sneezing, coughing, vomiting, laughing, or straining, may have the same effect.

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* Bruce Clarke, W.: Brit. Med. Journ., 1896, vol. ii, p. 1493.
† Glénard: Les ptoses Viscérales, Paris, 1899, p. 736 et passim.
‡ Steele, Dutton: Loc. cit.
§ Glénard: Les ptoses Viscérales, Paris, 1899, p. 503.
‖ Schwerdt: Deutsch. med. Wochen., Jan. 23, 1896.

Max Einhorn * refers to a singer on whom the laborious work of the diaphragm incident to his profession probably led to laceration of the hepatic ligaments.

Forms of Total Hepatoptosis.—In hepatoptosis the liver tends to be rotated in two different directions, (1) on its transverse axis, so that its upper (diaphragmatic) surface comes in contact with the abdominal wall, while the anterior surface points downwards; this is anteversion. (2) On its vertical axis; usually the convexity of the liver is turned to the right and the under surface to the left.

While the liver is more commonly displaced downwards and to the right, it may be displaced downwards and rotated to the left. Thus, the liver may be (1) simply anteverted; (2) anteverted with rotation to the right, the usual form; (3) anteverted with rotation to the left.

Hepatoptosis with Anteversion.—The liver being more fixed posteriorly, where the inferior vena cava runs through it, than elsewhere, movement is least in this situation. The liver moves downwards, the sharp anterior margin sinking down towards the pelvis while the superior or diaphragmatic surface slides forwards and downwards so as to come under the anterior abdominal wall. The inferior surface of the liver at the same time becomes more posterior. The liver becomes much flattened out and elongated. (*Vide* Fig. 9.) As the result of tight lacing, the front of the liver may show a transverse line of fibrous atrophy. This grooved condition of the liver (*le foie cordé; Schnurleber*) when exaggerated has been spoken of as the "pilgrim's bottle liver" ("*le foie en gourde de pélerin*").

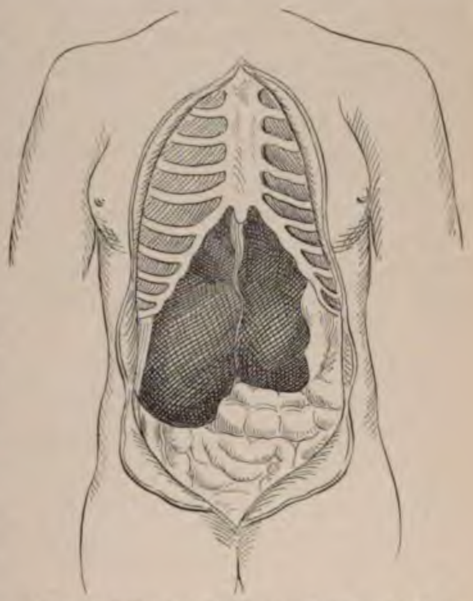

FIG. 9.—PARTIALLY ANTEVERTED LIVER WITH ELONGATION OF BOTH LOBES. (Drawn by Dr. H. B. Roderick.)

The following case, in which the condition was recognized only on the postmortem table, is a good example of hepatoptosis with anteversion.

On opening the body of a widow aged fifty who died of bronchitis after being only one day in St. George's Hospital, I found the liver extremely mobile, and occupying the front of the abdomen like a flattened cake and reaching 1½ inches below the umbilicus; both lobes were much elongated, as shown in the figure.

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* Max Einhorn: Medical Record, Sept. 16, 1899.

The coronary ligaments were very much elongated, measuring 2½ inches. There was also evidence of constriction from tight lacing; the lower part of the liver below the constriction could be easily turned up so as to form a double fold of liver substance. The commencement of the cystic duct contained a calculus, and the neck of the gall-bladder was much elongated. The kidneys appeared more movable than natural, and the presence of lineæ albicantes on the abdomen as well as the character of the os uteri made it probable that she had had children. This case was evidently one of partially anteverted wandering liver. Somewhat similar cases are described by Crawfurd,* Peters,† and Griffiths.‡

The following is a good example of a movable liver with rotation on its vertical axis to the right:

Morestin § found the gall-bladder and right lobe of a man's liver in the right iliac fossa. The liver was elongated and rotated so that the convexity pointed to the right and the under surface to the left. The left lobe was reduced in size to a mere tongue of hepatic tissue. There was no morbid change in the liver substance.

In cases of such rotation the right lobe may simulate disease around the appendix.

Complications.—Generally speaking, a movable liver can be replaced in its normal position, but this is not always possible; in 80 cases collected by Glénard this could not be effected in 14, while in 3 more it could only partially be accomplished. A movable liver may contract adhesions when displaced downwards, and so become fixed to the lower part of the abdomen. Under these circumstances it readily gives rise to great difficulty in diagnosis and may resemble some abdominal tumor or inflammatory formation.

Richelot,‖ in an exploratory laparotomy for an abdominal tumor of doubtful origin, found the liver rotated and fixed in the right iliac region.

A movable and displaced liver has been found to be cirrhosed, to be associated with calculous cholecystitis,** gall-stones, or in exceptional instances to be occupied by malignant disease or a hydatid cyst. (Nedwill.††) A certain amount of atrophy and subsequent fibrous substitution may be due to torsion and twisting of the portal vessels and bile-duct in the lesser omentum.

In 80 cases collected by Glénard ‡‡ the liver was healthy in 50; in 26 it was the subject of disease, usually cirrhosis or gall-stones. In one each cancer or hydatid cyst was present.

Physical Signs.—There is an abdominal tumor which is readily displaceable, and can be put back into the normal position of the liver, to which, indeed, it tends to return when the patient lies down, only to fall when a sitting or erect posture is assumed, the organ dropping two or more inches. The liver still descends on respiration; but the more marked the displacement, the less is this apparent. When the organ is very freely movable, and when presumably the lateral ligaments are greatly stretched or but ill developed, it can be readily rotated on its vertical axis, which passes through the inferior vena cava. This rotation is an exaggeration of that which a dilated stomach or colon may induce in the liver under normal conditions. The freedom of movement may, indeed, be so marked that the liver seems to turn over in its descent. When the patient turns on the left side, it travels in the same direction.

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* Crawfurd, R. P.: Lancet, 1897, vol. ii, p. 1182.
† Peters: New York Med. Gaz., 1882, p. 412.
‡ Griffiths, T. D.: Trans. Path. Soc., vol. xxviii.
§ H. Morestin: Bull. de la Soc Anat., Paris, 1896, p. 201.
‖ Richelot: Gaz. des Hôp., 1893, p. 783.
** Lennander: Gaz. des Hôp., May 10, 1900.
†† Nedwill: Lancet, 1901, vol. ii, p. 914.
‡‡ Glénard: Les ptoses Viscérales, Paris, 1899.

The displaced liver is visible under the relaxed abdominal walls as a rounded tumor on the right side about the level of the umbilicus. It is dull on percussion, firm, and smooth. The outline of the liver and perhaps the depression for the fundus of the gall-bladder and the notch between the left and right lobes for the round ligament can also be made out. When the organ has fallen away from the right hypochondrium, the normal liver dulness is replaced by resonance. In such cases the hand may be passed some way over the upper surface of the liver, between it and the diaphragm. There is a sinking or hollow in the right hypochondrium and a compensatory swelling or tumor, formed by the displaced liver, in the right flank or in the abdomen below the umbilicus. The empty state of the upper part of the abdomen below the right costal arch may be very striking.

The abdominal walls may be so lax and thin as to allow peristaltic action to be plainly visible, and divarication of the recti and a pendulous condition of the abdomen may be brought out when the patient rises from the horizontal position. According to Glénard, the lower part of the umbilicus becomes hidden by a fold of skin, upon which tension is brought to bear by the displaced liver through the attachment of the round and falciform ligaments. Other manifestations of visceroptosis, such as a floating kidney, a displaced uterus or stomach, may be present.

Onset.—Generally this is insidious and attracts no attention, but in some instances (Graham* says 5 per cent.) it may be sudden, and then resembles a traumatic dislocation. There is then a feeling of something giving way, accompanied by sudden, twisting pain, which may be so severe as to make the patient faint, and may then be regarded as biliary colic.

A good case of sudden dislocation of the liver is recorded by Garnett † in a woman aged fifty, who, when hurriedly stooping to pick something up from the floor, felt a sudden wrench in the right side of the abdomen. The liver was found reaching to the right iliac crest. Rest in bed and the application of an appropriate bandage were followed by recovery. Graham ‡ has seen a movable displaced liver due to the wheel of a wagon passing over the abdomen in a boy aged seventeen.

Symptoms.—The symptoms of floating liver may be summed up under different heads, as cases may present the features of one or more of the following symptom-groups:

(1) Pain, dragging, and heaviness in the hepatic region.

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* Graham, J. E.: Loomis and Thompson's System of Practical Med., vol. iii, p. 415.

† Garnett, A.: American Journ. Med. Sciences, 1881, p. 110.

‡ Graham, J. E.: Canadian Practitioner, 1895.

(2) Symptoms referable to the intestinal tract, viz., dyspepsia, vomiting, and mucous colic.

(3) Imitating biliary colic, viz., pain and jaundice.

(4) Imitating hepatic cirrhosis, viz., ascites, hæmatemesis, melæna. These symptoms are very rare.

(5) Symptoms belonging to the respiratory system, viz., cough, dyspnœa.

(6) Hypochondriasis, hysteria.

There may, however, be no symptoms at all.

Hepatic Pain.—When symptoms are present, the commonest is a feeling of discomfort, weight, or actual pain in the right hypochondrium. The dragging feeling is commonly felt in the right hypochondrium or epigastrium, but it may be more extensive and radiate behind the sternum or even to the base of the neck, the traction exerted on the diaphragm by the liver being perhaps transmitted through the pericardium to the cervical fascia. The pain and discomfort are usually relieved in the horizontal position, but are aggravated by movement, and may quite prevent the patient from walking or getting about, or even from lying on the right side. The pain, however, may be constant and very distressing, and is then quite probably due to chronic cholecystitis, cholelithiasis, or stretching of adhesions. There are frequently attacks of very severe pain, exactly like biliary colic, but not necessarily accompanied by jaundice.

In 44 cases of hepatoptosis these colicky attacks occurred in 37, or 84 per cent., and were only accompanied by jaundice in 14. (Dutton Steele.*)

This subject is referred to again later on.

Symptoms Referable to the Intestinal Tract.—In other cases the symptoms are mainly of a dyspeptic nature. Nausea and vomiting may occur and may be set up by lying on the right side. Intestinal disturbance, such as flatulent distension and constipation, may be present. Glénard † considers that the vascular disturbance resulting from a wandering liver is the cause of mucous or "membranous" colitis (or colic), which he thinks is often associated with enteroptosis. Probably many of the symptoms observed in hepatoptosis, such as hysterical mental disturbance and irritability, leucorrhœa, menorrhagia, albuminuria, are rather the results of enteroptosis in general than of hepatoptosis in particular.

Symptoms Imitating Biliary Colic.—As already mentioned, attacks of pain resembling biliary colic are very frequently met with in cases of wandering liver.

In 44 cases in which the liver was seen to be displaceable either at a laparotomy or autopsy, attacks of colic occurred in 37, or 84 per cent.; in 14 of these 37 there was jaundice and in 10 calculi. In 15 cases attacks of colic and transient jaundice occurred without gall-stones. (Dutton Steele.)

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* Dutton Steele: University of Pennsylvania Med. Bull., vol. xv, p. 424, Jan., 1903.

† Glénard: Académie de Médecine, April 20, 1897.

The colic may be due to at least three causes, viz., calculi, the presence of a floating kidney on the same side,* or torsion of one of the bile-ducts. In the absence of gall-stones and a floating kidney on the right side the attacks of colic are probably due to torsion of the cystic duct at its junction with the common bile-duct, which would not necessarily give rise to jaundice or to kinking of the common bile-duct at its commencement.

In Crawfurd's † case of hepatoptosis with jaundice a twist seemed to have occurred at the commencement of the common bile-duct. In this case I had an opportunity of examining sections of the liver which showed dilatation of the lymphatics and œdema in the portal spaces, as if the lymphatics had also been twisted and obstructed; but as bile had evidently passed into the general circulation, the obstruction must have been intermittent.

Dutton Steele discusses the question why jaundice is not always met with, and points out that the obstruction need not always be in the common bile-duct and that the kinking may be very transitory, the liver returning towards its normal position. His experiments showed that the further the liver was displaced towards the pelvis, the greater was the pressure required to drive an injection from the biliary papilla into the gall-bladder.

In some instances jaundice may occur without pain; Steele refers to two cases. It may be catarrhal, as in Snowman's ‡ case.

It may be pointed out that a displaced liver may by traction on the ducts lead to stagnation of bile in the ducts, and so favour hydrops of the gall-bladder, cholecystitis, and the production of gall-stones.

In Newman's § case the gall-bladder contained thirty ounces of straw-coloured fluid and numerous gall-stones.

Symptoms Imitating Hepatic Cirrhosis.—As very exceptional results, reference may be made to the occurrence of ascites, probably caused by twisting of the portal vein, and œdema of the legs, probably due to a kink of the inferior vena cava. Twisting of the portal vein, by obstructing the circulation, might be expected to give rise to venous oozing into the stomach and intestines and so to hæmatemesis and melæna. Hæmatemesis is, however, extremely rare.

McNaughton Jones ‖ describes a case of a woman aged thirty-eight, the mother of seven children, who had hæmatemesis on several occasions, the first at the age of nineteen. The last attack was very severe, and at this time a tumor, thought to be renal, was discovered. At the laparotomy the tumor was found to be liver, which extended into the right iliac fossa.

Symptoms Referable to the Respiratory System.—In some cases classed by Max Einhorn ** as asthmatic there is dyspnœa in addition to a feeling of fulness and constriction in the upper part of the abdomen.

A dry cough of eighteen years' duration, which, however, disappeared when the patient was in the recumbent posture, was found by L. Vène †† to be associated

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[*] Compare J. Hutchinson, Jr.: Practitioner, Feb., 1902.

[†] Crawfurd: Lancet, 1897, vol. ii, p. 1182.

[‡] Snowman: Lancet, 1896, vol. i.

[§] D. Newman: Brit. Med. Journ., 1902, vol. ii, p. 249.

[‖] McNaughton Jones: Lancet, 1898, vol. i, p. 1327.

[**] Max Einhorn: Medical Record, Sept. 16, 1899.

[††] Louis Vène: Journal de Médecine Interne, Oct. 15, 1898.

with hepatoptosis, and was cured by the application of a flannel bandage. It was thought that the cough was due to excitation of the diaphragm by traction of the liver on the inferior vena cava.

Some instances of cough usually put down to hysteria may in reality be due to hepatoptosis.

Hysteria or hypochondriasis is frequently observed to be associated with hepatoptosis; the mental depression may result in the patient acquiring the morphia habit.

Absence of Symptoms.—A freely movable liver may be found accidentally in patients who do not suffer any inconvenience from it. Beddard * refers to a case in a placid unmarried lady who lived at her ease and in whom "the tumor" formed by the prolapsed liver merely aroused an "amused curiosity." It is probable that the presence or absence of symptoms largely depends on the life the individual leads and on her temperament. Women of a high-strung and nervous nature often feel pain and suffer inconvenience from conditions, such as peritoneal adhesions and floating kidneys, of which their more robust sisters are unconscious.

Diagnosis.—In some cases where movable livers have been felt clinically the organ has at the postmortem examination been found in its normal position, so that a doubt has naturally been thrown on the correctness of the diagnosis. But if in such a case the suspensory ligaments are found to be much elongated, it is quite possible that the organ has returned to its natural condition as the result of collapse of the lungs and ascent of the diaphragm, on the one hand, and gaseous distension of the intestines, on the other hand, pushing the liver up.

The chief points in the diagnosis are the presence of a movable abdominal tumor, resembling the liver, which can be replaced in the position of that organ, and the fact that the hepatic region is sunken and resonant on percussion when the tumor is in the middle of the abdomen. In addition, other conditions, such as a floating kidney, etc. (*vide* Differential Diagnosis), must be excluded.

Differential Diagnosis.—A freely movable or wandering liver must be distinguished from an enlarged liver, from a tongue-like lobe with or without a distended gall-bladder, and from mere downward displacement of the liver such as may result from pleural effusion, pneumothorax, or other causes.

In Packard's † case of movable liver the diagnosis during life was subphrenic abscess following typhoid fever.

From Floating Kidney.—The most frequent mistake seems to consist in regarding a wandering liver as a floating kidney or as some other form of enlargement of the right kidney. Floating kidneys are much commoner than hepatoptosis, and the general symptoms are so much alike that the condition of the liver may be overlooked, especially when, as is by no means infrequent, there is a floating kidney as well as a wandering liver. Alteration in the position of a floating liver may imitate an intermittent hydronephrosis, while concomitant distension of the gall-bladder may have the same effect.

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* Beddard, A. P.: Guy's Hospital Reports, vol. lvii, p. 179, 1902.

† Packard: Trans. Coll. Physicians, Philadelphia, 1896, p. 230.

Newman * operated on a floating liver and let out 30 ounces of bile from the gall-bladder. The symptoms had suggested a hydronephrosis.

A careful bimanual examination, if necessary under an anæsthetic, should be made; the liver dulness should be percussed, and an attempt to displace the abdominal tumor into the right loin should be made.

From Tumors and Hydatid Cysts in the Liver.—A wandering liver may suggest malignant disease of the organ, especially when, as in rare cases like Crawfurd's,† jaundice and ascites are present from torsion of the common bile-duct and portal vein in the lesser omentum. The ease with which the liver is displaced ought to prevent any mistake of this kind, while, on the other hand, irregularities of the surface of the liver and signs of chronic obstruction of the colon make malignant disease probable.

Hydatid cysts projecting from the upper surface of the liver, or, in rare instances, between the liver and diaphragm, give rise to downward displacement of the organ, but there is no absence of the hepatic dulness below the sixth rib in the right nipple line, as there would be if the liver had dropped away from its normal position. The converse mistake has occurred, and laparotomies undertaken for supposed hydatid cysts have led to the discovery of a wandering liver. (Marchant ‡, Areilza.§)

Gall-stones.—The pain and jaundice, presumably due to twisting of the bile-duct, may give rise, as in a case of Mathieu's,‖ to a diagnosis of biliary colic. Max Einhorn ** has seen five cases of wandering liver that had previously been erroneously diagnosed as cholelithiasis. The two conditions may both be present.

Tumors and Inflammatory Thickenings of the Omenta, Mesentery, etc.—Tumors and cysts of the omentum and of the mesentery, though movable, cannot be displaced to the same extent from above downwards as a wandering liver; moreover, they are separated by a zone of resonance from the liver dulness. Inflammatory thickenings in the omentum are comparatively fixed and are hardly likely to give rise to any difficulty in diagnosis.

In some exceptional cases it is just conceivable that a question might arise whether a movable tumor is the liver or a mass of growth in the stomach, colon, or inflammation around the appendix; but under ordinary conditions there is little or no resemblance between hepatoptosis and these conditions.

Treatment.—Tight lacing and corsets which constrict the lower part of the thorax and tend to displace the liver downwards must be discontinued. The "straight-fronted" corset should be worn, as it supports the abdomen from below and does not compress the waist unduly. A suitable abdominal belt, binder, or elastic bandages should be applied so as to support the lower abdomen in an upward direction, and thus, by increasing the intra-abdominal pressure, to support the liver in its proper position. The belt or binder must reach below the hips and should be fixed in position while the patient is still in bed in the morning and before the liver has become prolapsed. This method of replacing the healthy tone of the abdominal muscles is much more effective than applying a supporting pad to the liver alone. The treatment of movable liver is on the same lines as that of enteroptosis or Glénard's disease.

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* Newman: Brit. Med. Journ., 1902, vol. ii, p. 249.
† Crawfurd, R.: Lancet, 1897, vol. ii, p. 1182.
‡ G. Marchant: Acad. de Méd., Paris, Aug. 11, 1891.
§ Areilza: Rev. Med. y Cirug. pract., 1896.
‖ Mathieu: Gaz. des hôp., 1893, p. 1152.
** Max Einhorn: Medical Record, Sept. 16, 1899.

Diet is a matter of importance and, as a rule, the patient requires liberal feeding so as to improve the general state of nutrition. The subjects of hepatoptosis are usually weakly, but when there is decided corpulence, the amount and quality of food taken should be supervised by the medical attendant, and any excessive eating interdicted. There will be no difficulty in distinguishing the weakly, flabby patient whose muscles and tissues are in want of better food from the heavy eater whose liver and tissues are congested from the presence of the products of excessive proteid metabolism. It is important to keep the bowels freely open, for in this way portal congestion and flatulent distension are relieved and a distended gall-bladder may be emptied, conditions which may conceivably dispose to or exaggerate hepatoptosis.

In order to improve the tone of the abdominal muscles carefully planned gymnastic exercises may be employed. The exercises should be simple and readily carried out. Lea* speaks of the following as very efficient:

(1) The patient lies on the back without any pillows, the arms being folded in front, and gradually raises herself into the sitting posture without any help from the arms.

(2) The patient, being in the same position as before, raises first one lower limb, then both, with the knees extended, to a right angle with the trunk.

(3) Deep breathing, especially inspiratory movements with the glottis closed and after a forced expiration. This exercise is useful in drawing up the viscera.

Lea directs that each of these exercises should be performed six to twelve times night and morning.

Massage may be used in order to improve the muscular tone.

Electrical stimulation has been applied to the abdominal muscles and has been found to be beneficial. Griffith † obtained a good result by daily stimulating the muscles with an interrupted current for three months, but the long duration of the treatment would render it unsuitable in many cases.

If the application of a belt and the other palliative measures referred to fail to relieve the symptoms, and the pain is so severe as to incapacitate the patient from ordinary life and work, the advisability of surgical interference must be considered. The operation of fixing the liver by sutures or other means in its proper position is known as hepatopexy or hepatorrhaphy. Various methods have been adopted, such as passing sutures through the liver substance and the abdominal wall, tying the round ligament up to the cartilage of the seventh rib and at the same time promoting adhesions between the diaphragm and convexity of the liver by rubbing the peritoneum with aseptic gauze. When the gall-bladder contains calculi, the operation for cholecystotomy usually leads to fixation of the liver.

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* A. W. W. Lea: Medical Chronicle, July, 1902.

† Griffith: Brit. Med. Journ., 1878, vol. i, p. 89.

In 1891 Gérard Marchant * fixed the anterior margin of the liver to the costal margin by four silk sutures, and was followed by Langenbuch † and Richelot,‡ who performed somewhat similar operations. Treves § utilized the round ligament to support the sutures. Lannelongue and Faquet ‖ in 1895 sutured the liver to the anterior abdominal wall and roughened the opposed surfaces of the liver and diaphragm so as to get adhesions. Union of the liver to the opposed peritoneal surface of the diaphragm has also been obtained by swabbing the surface of the liver with strong carbolic acid.

Péan ** supported the liver by uniting the peritoneum of the anterior abdominal wall with that of the postero-lateral part of the abdomen below the replaced liver.

In fifteen cases of hepatopexy collected by Terrier and Auvray †† there were eleven cures.

The drawbacks to operative measures are,—(1) that the underlying condition disposing to enteroptosis in general and hepatoptosis in particular is not removed; (2) that the incision through the abdominal walls is very prone to become the seat of hernial protrusion, inasmuch as their tone and nutrition are especially defective.

On the other hand, hepatopexy may succeed after all other mechanical and palliative measures have failed, and it does so by compensating for, though not removing, the disposing factors of hepatoptosis. The danger of hernial protrusion in the scar is probably greater in old women with permanently pendulous abdomens than in younger women who are temporarily in a low state of nutrition from several rapidly succeeding pregnancies. In any case an abdominal belt should be worn after the operation.

With regard to prophylaxis, the practice of tight lacing should be prevented and care should be taken that a pendulous condition of the abdominal wall is not induced or aggravated by getting up too soon after parturition and by neglecting the use of a proper binder.

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* Gérard Marchant: Acad. de Méd., Aug. 11, 1891.

† Langenbuch: Deutsch. med. Wochen., 1891, S. 1241.

‡ Richelot: Gaz. Hebd. de Méd. et de Chirurg., 1892, p. 242.

§ Treves: Brit. Med. Journ., Jan. 4, 1896.

‖ Lannelongue et Faquet: Congrès de Bordeaux, 1895. Quoted by Treves: Lancet, 1900, vol. i, 1344.

** Péan: Congrès de Chirurg., Paris, 1896. Quoted by Treves: Lancet, 1900, vol. i, 1344.

†† Terrier et Auvray: Rev. de Chirurg., 1897, p. 746.

FUNCTIONAL DISEASE OF THE LIVER.

Before entering on the rather difficult subject of functional disease of the liver it will be convenient to enumerate the important functions of the liver.

(1) The secretion of bile.

(2) The metabolic processes in connection with the formation, storage, and supply of glycogen.

(3) In connection with proteid metabolism. The liver is very largely concerned in the conversion of ammonia into urea, but there is no reason to believe that it plays any part of importance in the production of uric acid. In some diseases, in which the liver cells are degenerated, the amount of urea is diminished while the quantity of nitrogen excreted in the urine as ammonia is increased. It has, therefore, naturally been assumed that the fall in the output of urea was due to failure in the functional activity of the liver cells. This, however, is not the true explanation. The real reason is that in these diseases organic acids, of the fatty acid series, are formed and unite with any available bases, among which is ammonia, present in the blood. The ammonia, which under ordinary conditions would be changed by the liver into urea, is now in a form which cannot undergo this transformation, and therefore appears in the urine linked with an organic acid. This occurs in acute yellow atrophy, phosphorus poisoning, and some cases of cirrhosis and fatty liver. In such cases ammonia given by the mouth increases the amount of urea in the urine, thus showing that the liver cells have not lost their power of transforming ammonia into urea. It is only in the very latest stages of such diseases, shortly before death, that the liver cells appear to lose this power.*

(4) Its antitoxic or protective function. Poisons, whether introduced into the alimentary canal or manufactured there as the result of bacterial activity, are normally arrested, or converted into harmless bodies by the liver cells. The detoxicating action of the liver is shown by the difference in the action of poisons, such as strychnine, conia, snake poison, albumoses, when introduced into the portal circulation, on the one hand, and into the general circulation, on the other hand. It appears from Roger's † observations that the antitoxic function of the liver varies with its richness in glycogen and its power of stopping sugar and forming glycogen, and that if the liver loses its power of stopping sugar it is also unable to arrest poisonous bodies brought to it from the portal area. In complete biliary obstruction the antitoxic power of the liver fails, and the grave manifestations seen under these conditions are chiefly due

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* For a lucid account of this question the reader should refer to Herter's Lectures on Chemical Pathology, p. 338.

† Roger: La Presse Médicale, June 26, 1897.

to the poisons which flood the body, and only depend in a minor degree on the presence of the bile pigments in the blood.

From the number and importance of the functions of the liver it is clear that failure in discharge of these duties must be followed by very definite symptoms. Functional disturbance is undoubtedly common in the liver, but the following questions require some consideration:

(1) Are the disorders of hepatic function primary in the liver? and (2) Are they entirely independent of structural change in the organ?

Numerous conditions, many of them in no way connected with the liver, were formerly described as due to functional disease of that organ. The idea was attractive to the lay mind and is recklessly appealed to in everyday life. Flatulence, dyspepsia, constipation, and the bad effects of overeating and drinking are often euphemistically described as "liver." As a reaction against this inaccurate though comforting doctrine the tendency at the present time among most English medical writers is to ignore the subject or to deny the existence of primary functional disease of the liver. This swing of the pendulum to the opposite extreme —for it must be admitted that the idea originated with the profession— is due to the knowledge that the symptoms ascribed to functional disease of the liver can in great part be explained as due to other factors, such as indigestion, auto-intoxication, constipation, or to subacute congestion or even inflammation of the organ, often secondary to intestinal disturbance or to absorption of toxic products from the intestine. In other words, the hepatic disturbances formerly regarded as due to primary functional insufficiency are in the vast majority of cases dependent on morbid processes elsewhere, and therefore secondary, or are associated with definite organic change in the liver.

Thus, to consider the symptoms commonly referred to functional disorder of the liver, the distaste for food, dyspepsia, flatulence, constipation or diarrhœa, are the expression of gastro-intestinal catarrh set up by poisonous or unsuitable food. The icteric tint of the conjunctivæ, the muddy skin, and some of the mental depression are either due to the spread of the gastro-duodenal catarrh to the biliary papilla and the slight obstruction to the flow of bile thus induced; or possibly to catarrh of the minute intra-hepatic ducts set up by poisons absorbed from the alimentary canal and subsequently excreted into the ducts; and in either case to the passage of bile, which often contains toxic constituents, into the general circulation. The pale colour of the fæces may be due to catarrh of the bile-duct and a deficient amount of bile, but in cases where there is no evidence of jaundice elsewhere it is often the result of the fæces being permeated with bubbles of gas from excessive carbohydrate fermentation. This colour of the fæces is often mentioned by the patients as proof that "the liver is not acting" and that there is an imperfect formation of bile.

The headache, giddiness, muscæ volitantes, malaise, muscular debility, mental depression, and irritability are due to the local action on the nervous system of poisons absorbed from the alimentary canal. These toxic bodies are either produced in such quantities that the liver fails to stop them, or more probably they act on the liver cells and impair their vitality and function; in either case the general circulation becomes flooded with toxic bodies. The piles, the feeling of weight in the right hypochondrium, and shoulder pain depend on hepatic congestion or even slight hepatitis brought on by constipation and the advent to the liver of digestive products in excessive amounts and probably of altered (*i. e.*, toxic) quality. This state of hepatic congestion is especially apt to be set up in patients who have suffered from malaria in the tropics. (*Vide* Tropical Liver.) Nevertheless there can be no doubt that in some instances morbid results are referred to the functional disturbance of the liver without its being always possible to determine satisfactorily that this disturbance is secondary. Thus, in some forms of glycosuria it is possible that there is an excessive activity of the glycogenic function, while again in alimentary glycosuria the liver fails to discharge efficiently its function of stopping the sugar brought to it by the portal vein. As a rule, in alimentary glycosuria there is some definite underlying cause, such as pancreatic disease, but it cannot be recognized in all cases. These conditions, however, are not ordinarily spoken of as functional disease of the liver.

It has recently been urged that puerperal eclampsia is in many cases due to hepatic insufficiency, and that the renal symptoms are secondary to a primary hepatic toxæmia. During pregnancy toxæmia is favoured by several factors, such as the retention of bodies which are normally removed in the menstrual flow, the passage of toxic bodies, derived from metabolic processes in the fœtus, into the maternal circulation, and auto-intoxication from constipation, which is so common during pregnancy. In a woman who inherits a diminished hepatic activity and resistance the liver fails to rise to the occasion and to stop and destroy the poisons which reach it. The blood then becomes flooded with poisons, and symptoms of toxæmia result. These are dyspepsia, severe vomiting, ptyalism, œdema without albuminuria, pruritus, and pigmentation. In more marked instances there are intractable vomiting, jaundice, acute yellow atrophy, mania, eclampsia, etc. In fatal cases, however, changes are constant in the liver, and consist in focal or more extensive necroses, degeneration of the liver cells, and hæmorrhages.

As has already been admitted, functional disorder of the liver is no doubt responsible for many symptoms. The difficulty in regard to the subject is to prove that the functional disturbance is primary in the liver and not secondary to disease or morbid factors elsewhere. The discussion is not a mere academic exercise, but has a practical bearing on the treatment. Thus, if it were thought that there was a primary failure of hepatic activity, as is implied by the common phrase "torpid liver," the rational course would be to stimulate the organ. Whereas, if there was an underlying and primary factor elsewhere, this should be attacked.

The difficulties about the recognition of primary functional disorders of the liver may be best explained by referring to some of the conditions which it has been supposed to cause.

Lithæmia was described by Murchison[*] as a condition of innate defect of power, often hereditary, in the liver, in virtue of which its healthy functions are liable to be deranged by the most ordinary articles of diet. As a result of this hepatic insufficiency uric acid, instead of urea, was said to be produced in the liver and turned out into the blood. Among the results of lithæmia Murchison enumerates such different conditions as dyspepsia, constipation, gout, urinary calculi, biliary calculi, and acute and chronic renal disease.

This conception has been revived in France under a different name—"hepatism"—by Glénard[†] It is regarded as a chronic nutritional change which may be hereditary or acquired. It may take (*a*) the cholæmic form; this condition is much the same as the simple family cholæmia more recently described by Gilbert and Lereboullet,[‡] in which the blood-serum contains bile-pigment though the urine usually does not. Its primary signs are pigmentation of the skin, which may be of the nature of slight jaundice, or dark and resembling Addison's disease, moles, freckles, or brown areas (the biliary mask) resembling the melasma of pregnancy, and xanthelasma of the eyelids. As secondary results such various conditions as the following may arise: dyspepsia, abdominal pain, hæmatemesis, epistaxis, mucous colitis, megrim, albuminuria, and rheumatic pains, while it is closely related to transient and chronic jaundice, biliary cirrhosis, and similar conditions. (*b*) The uricæmic form, which corresponds to the diathesis termed "arthritism" by some French writers, or to Murchison's lithæmia. A mixture of these two forms corresponds to the diathesis of "herpetism" described by some French writers. Hepatism, according to Glénard, is a functional disturbance of the liver and is the cause of a large number of diseases, including those incriminated by Murchison, and, in addition, neurasthenia, diabetes, chlorosis, and visceroptosis. It may be pointed out that the cholæmic form is probably dependent on slight catarrh of some part of the bile-ducts, either in the liver or close to the termination of the common bile-duct in the duodenum.

Murchison's theory of lithæmia is very far-reaching, and among other things offers an explanation of gout; in fact, many of the manifestations of lithæmia are those of irregular gout. Among recent writers Yeo[§] has supported the view that hepatic inadequacy is an underlying factor in the production of gout. The protean manifestations of neurasthenia include many of those formerly ascribed to functional failure on the part of the liver.

This theory of lithæmia depends on the assumption that as the result of imperfect metabolism uric acid, instead of urea, is manufactured by the liver. There are two mistakes here. In the first place, it is now universally agreed that uric acid and urea are the products of entirely distinct metabolic processes, and that there is nothing to support the view that if the formation of urea is left incomplete uric acid results. As Woods Hutchinson[‖] graphically expresses it, they are practically as distinct from each other as the urine from fæces. In the second place, it has been shown since Murchison's time that the liver does not play any predominant part in the manufacture of uric acid. Uric acid is produced in the body generally, and more especially from lymphoid tissue; it is closely associated with leucocytosis, uric acid being derived from the nuclein of the cells. This is well seen in the excessive excretion of uric acid in leukæmia. According to P. W. Latham, Kolisch, and Luff,* uric acid is manufactured in the kidneys. It is, therefore, too narrow a view of the faulty metabolism of proteid material which results in an excessive production of uric acid to say that it depends on functional disorder of the liver to the exclusion of the rest of the body.

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[*] Murchison, C.: Croonian Lectures; Royal College of Physicians, 1874. Diseases of the Liver, p. 594, ed. ii, 1877.

[†] Glénard: Les ptoses Viscérales, Paris, 1899.

[‡] Gilbert and Lereboullet: Gaz. Hebdom. de Méd. et de Chirurg., Sept. 21, 1902, p. 889.

[§] Yeo: Brit. Med. Journ., 1901, vol. i, p. 1457.

[‖] Woods Hutchinson: Lancet, 1903, vol. i, p. 288.

Habitual high arterial tension and its accompaniments, such as migraine, might be thought to depend on a failure of the liver to stop and destroy the poisonous bodies that are continually being carried to it from the intestines. The liver undoubtedly exerts this important function of protecting the body from auto-intoxication, but it is difficult to prove that failure in the discharge of this duty leads to high arterial tension; since in cases of extensive disorganization of the liver—for example, in cirrhosis—hepatic insufficiency must exist, but the arterial tension is low and not raised. It is much more likely that high arterial tension is, like gout, due to some general disorder of metabolism of the body.

In cases popularly described as "biliousness" or "torpid liver" the symptoms are indigestion, some hepatic pain, headache, slight icteric tingeing of the conjunctivæ with an apparent or real deficiency of colouring-matter in the fæces. The most probable explanation of these symptoms is gastro-duodenal catarrh with slight catarrhal jaundice and not a primary diminution in the secretion of bile. In these cases it is possible either that there is catarrhal swelling of the biliary papilla in the duodenum or that, as the result of indigestion, poisonous products are carried to the liver and then, when excreted into the bile-ducts, set up a certain amount of catarrh in the small intra-hepatic ducts. This leads to reabsorption of the bile with the poisons contained in it, which pass into the general circulation and act on the body as a whole. Sir Lauder Brunton † has shown that it is probable that the proverbial bitter taste of the bile is pathological and due to the presence of poisons absorbed from the bowel and then excreted into the ducts, and that in health the bile is tasteless.

It must be borne in mind that the liver, like other organs, must vary greatly in different individuals as to its functional activity and reserve power, and that an amount of food-products which can be satisfactorily dealt with by the liver in one individual would in another be entirely beyond its capabilities. This difference in the inherent powers of the liver in different persons is analogous to variations in their muscular and mental powers, and the less powerful should not be described as suffering from functional disease of their muscles or brain because they fail to accomplish the work which their better developed companions have no difficulty with. If, therefore, an individual consumes an amount of food that is excessive for his powers of digestion, fermentation and auto-intoxication will result. These poisons will impair the functional activity of the liver, and as a result the poisonous products of digestion will be allowed to pass into the general circulation and give rise to the various toxic manifestations already referred to. From what has gone before, it is evident that the well-known symptoms ascribed to a "torpid" or "inactive liver" are chiefly due to factors which secondarily interfere with the functional activity of the liver and not to a primary functional failure on the part of that organ. But because the ingenious conception of lithæmia and other views as to primary functional disease of the liver do not commend themselves in the light of later knowledge, it does not follow that hepatic insufficiency or inadequacy is a negligible factor. It is quite possible that primary functional disorder of the liver does occur, but in the present state of our knowledge its existence is almost impossible to recognize with accuracy.

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* Luff, A. P.: Practitioner, March, 1898.

† Sir T. L. Brunton: Clinical Journ., Jan. 10, 1900.

The symptoms of secondary functional disturbance of the liver have already been referred to (p. 41); a few lines as to their treatment will now be given.

Treatment.—The treatment of the symptoms of secondary hepatic inadequacy must therefore be directed to the causes and not to the liver itself. In the first place, the alimentary canal should be cleared out; this is most satisfactorily effected by the use of calomel, grs. iij, or of the old-fashioned blue pill, grs. v, followed by haustus sennæ, or saline purgatives, such as sulphate of magnesium or soda, phosphate of soda, or some natural mineral water with purgative properties. The mercury drives the bile out of the gall-bladder, unloads the bile-ducts, and by sluicing the common duct tends to remove the causes of catarrh of its lower end. At the same time it acts as an intestinal antiseptic and inhibits excessive fermentation, and thus puts a stop to further auto-intoxication. The saline removes the mercury from the intestinal surface and prevents prolonged irritation, while at the same time it diminishes portal engorgement. The purgative action of these two remedies removes poisons from the alimentary canal. Intestinal fermentation and putrefaction can be most satisfactorily prevented by careful dieting and by the administration of minute doses of calomel ($\frac{1}{40}$ to $\frac{1}{20}$ grain) three times a day, which is preferable to salol, β-naphthol, and other popular drugs employed for this purpose. It is, of course, important that the bowels should be kept properly open. The ordinary purgatives already mentioned may be used for this purpose, or a pill containing euonymin and iridin. These two drugs are often employed and spoken of as if they had some special action other than that of purgatives, but without any satisfactory reason.

Plenty of water should be taken so as to wash out the poisonous products from the circulation and stimulate the functional activity of the kidneys. It is better not to take water in considerable quantities either with or directly after food, but to take it one-half an hour or so before a meal. Hot water may be sipped first thing in the morning and last thing at night. During the existence of symptoms a liquid diet, of which milk is the staple, should be adopted, while alcohol in any form should be rigidly avoided. In the second place, the patient should be warned to avoid the forms of food likely to set up intestinal catarrh and fermentation. The articles of food that must be avoided as indigestible will, of course, vary in individual cases, but, generally speaking, the following should be forbidden: Concentrated and highly spiced soups; rich fish, such as salmon, mullet, eels, kippered fish; duck, hare, made dishes, entrées, pickles, rich sauces, melted butter, tea cakes, crumpets, sweets, cream, cheese, and much proteid food. Alcohol should be avoided or taken in great moderation, well diluted, and with meals. Claret, hock, or whisky are the forms that may be taken if it is thought desirable, but beer, stout, cider, champagne, sherry, Madeira, Port, Burgundy, and liqueurs should be strictly prohibited.

Exercise is important. The form of exercise most suitable to individual requirements varies somewhat, and a stereotyped direction cannot be given to all cases. In some instances where the symptoms have existed for a considerable time and where muscular debility is present, active exercise is unsuitable, at any rate at first, and may lead to exhaustion and exaggeration of the symptoms. Under such circumstances massage may give very good results and may be followed by carefully regulated exercise, such as Ling's Swedish gymnastics. In ordinary cases, however, massage and gymnastics are hardly necessary. In some persons walking briskly is sufficient, but in many, probably in the majority, a more active form of exertion is more effective, such as horse-riding, bicycling, golf, or lawn tennis. There is the additional advantage that these forms of exercise distract the attention from the individual's private business or worries. Open-air exercise is better than indoor, but when the weather is bad, fencing, racquets, boxing, or gymnastics may be of great use in improving the conditions of health.

It is important to get the skin to act, and for this purpose Turkish baths or hot baths with vigorous friction of the skin by rough towels are useful. When the skin has been acting vigorously after exercise the underclothing should be changed as soon as the individual comes in, so as to avoid chilling the surface of the body. The body should be well but not too warmly clad, and care must be taken to avoid chills to the legs, abdomen, and neck.

A visit to a spa, either in this country, such as Harrogate, Llandrindod Wells, or Strathpeffer, or abroad, Homburg, Ems, Neuenahr, Vichy, Carlsbad, Marienbad, etc., may be followed by improvement or cure. The patient not only undergoes a carefully regulated course of treatment ("the cure"), but gets change, holiday, and rest from the cares of business or other worries.

As to the prognosis, the digestive disturbances which give rise to these symptoms are much the same as those leading to cirrhosis, and indeed the symptoms of functional disease of the liver may in some instances be the early manifestations of cirrhosis. As a rule, however, the prognosis is good provided the patient conforms to medical advice.

DISEASES OF THE HEPATIC ARTERY.

Aneurysm; Embolism; Thrombosis; Arteriosclerosis; Etc.

ANEURYSM.

Aneurysms of the hepatic artery have been recorded in rather more than twenty instances; but examination of metropolitan and other museums would increase the number of cases; thus there is a large hepatic aneurysm, the size of a cocoanut, in the Museum of Surgeon's Hall, Edinburgh, and another the size of a turkey's head in the Museum of St. George's Hospital.

Age and Sex.—In 24 cases where the ages were given, the average age was 34.5 years, the extremes being 56 and 17 years. In 24 cases, 8 were females and 16 males. The average age in the women was a little higher (36 years) than in the men (33.5).

Causation.—Some of these aneurysms may be due to embolism, and from the comparatively unsupported condition of the visceral arteries in the abdominal cavity, simple non-infective embolism is more likely to be followed by aneurysm there than in other situations, except, perhaps, in the circle of Willis, where the arteries lie on a yielding water-bed, the subarachnoid space. Traumatism has been noted as a cause of hepatic aneurysm; thus, Mester's * patient was kicked in the abdomen by a horse. In most cases of hepatic aneurysm there is no evidence of embolism or traumatism and yet these factors seem more probable than mere chronic endarteritis. Perhaps in some instances the cause of the embolus, such as a calcareous plate from the aorta, has naturally been overlooked, or has passed away before the patient's death. Often, however, no antecedent condition, except endarteritis, is recorded.

A very interesting specimen of an aneurysm the size of a walnut was found by the late Dr. Pearson Irvine † inside an abscess in the left lobe of the liver; here the aneurysm was produced by inflammation and ulceration of the outer coats of the artery in the same way that aneurysms are formed in vomicæ during the course of pulmonary tuberculosis.

Aneurysms of the hepatic artery or its branches may be due to ulceration starting in the walls of the gall-bladder or the bile-ducts and eroding the wall of the artery. At first an aneurysm would result, and later, by extension of the ulceration, the aneurysm would be opened into the bile-duct.

This ulceration may be due to gall-stones. Naunyn ‡ regards Lebert's case of rupture of an hepatic aneurysm into the gall-bladder of a woman aged thirty, with fatal gastro-intestinal hæmorrhage, as due to gall-stones, and quotes M. B. Schmidt's case of ulceration of the bile-duct, in connection with an impacted gall-stone, opening into an aneurysm of the hepatic artery. Schmidt has recently reported another case in which cholelithiasis probably set up ulceration of the gall-bladder and an aneurysm of a branch of the hepatic artery.

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* Mester: Zeitschrift f. klin. Med., Bd. xxviii, S. 93, 1895.

† Pearson Irvine: Trans. Path. Soc., vol. xxix, p. 128.

‡ Naunyn: On Cholelithiasis, p. 141. Translation, New Sydenham Soc.

In connexion with the production of hepatic aneurysm by ulceration starting in the gall-bladder or bile-ducts and possibly due to cholelithiasis, it is significant that in 24 cases of hepatic aneurysm where the sex is noted 8 were in women and 16 in men. Aneurysms are so rare in women, while gall-stones are so common, that it is probable this large proportion of female cases in aneurysm of the hepatic artery may to some extent be due to the mechanism of ulceration of the artery from without. Usually there is a single aneurysm on the trunk or extra-hepatic branches of the hepatic artery, but in some instances more than one or even multiple aneurysms have been recorded.

In a boy aged seventeen there were two intra-hepatic aneurysms (Borcher*), and in a boy aged eighteen Hale White † found an aneurysm on each of the main branches of the hepatic artery, one of which was embedded in the substance of the liver. Multiple aneurysms of small size may occur in great profusion in the liver in the rare disease periarteritis nodosa. Intra-hepatic aneurysms have, however, attracted very little attention, and are very rarely seen.

Symptoms of Hepatic Aneurysm.—Pain is nearly always present, and may be mistaken for that of biliary colic; in fact "pseudo-biliary" colic may be due to the pressure of the aneurysm on the bile-ducts. Jaundice, from pressure on the bile-ducts, very frequently occurs, though the jaundice may be slight and not appear until late in the course of the disease. Aneurysm and new-growth in the portal fissure behave, in a miniature fashion, just as the corresponding lesions in the anterior mediastinum do with regard to the adjacent venous trunks. Aortic aneurysm rarely obstructs the superior vena cava, while mediastinal growth frequently does. In the same way aneurysm of the hepatic artery, though it may push the portal vein aside, does not obliterate it or give rise to ascites.

Hepatic aneurysm may perforate into the peritoneum and give rise to fatal collapse. Usually it ruptures into some part of the bile-ducts, and the blood thus poured out passes into the alimentary canal and may be vomited, or more often passed by the bowel alone; repeated leakage and hæmorrhages may occur before a fatal one. Rupture of the aneurysm may take place into the hepatic or common bile-ducts, the gall-bladder, colon, and possibly stomach.

A pulsating tumor may be felt in the epigastrium, and a bruit may be heard over it.

Aneurysm of the hepatic artery, as in a case recorded by Ledieu, may obstruct the circulation in its branches. By experimental ligation of the hepatic artery in dogs Dujarier and Castaigne ‡ have found that the flow of bile is retarded and that infection of the bile-ducts is thus rendered more easy. This may explain cases where multiple abscesses in the liver are found associated with an aneurysm of the hepatic artery.

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* Borcher: Aneurysma d. Art. hepat., Kiel, 1878.

† Hale White: Brit. Med. Journ., 1892, vol. i, p. 223.

‡ Dujarier and Castaigne: Bull. Soc. Anat., Paris, 1899, p. 329.

Ross and Osler[*] have recorded a remarkable case where the sac of an hepatic aneurysm became septic and multiple emboli passed into the liver, leading to numerous abscesses.

Diagnosis.—The diagnosis of hepatic aneurysm is very difficult. Most of the recorded cases have been regarded as duodenal ulcer or cholelithiasis. It would be very difficult to distinguish with certainty between an hepatic aneurysm and one of the abdominal aorta in the immediate neighbourhood; especially as the latter may press on the bile-duct and give rise to jaundice.

Treatment is usually merely palliative. Of four cases treated surgically, three died; in the fourth, which recovered, Kehr[†] successfully ligated the hepatic artery and removed the aneurysm.

EMBOLISM.

Embolism of the main trunk of the hepatic artery is very rarely observed; possibly it is sometimes missed, from the fact that the artery is not systematically examined. Chiari[‡] in a case of embolism involving the main trunk of the hepatic artery found complete necrosis of the liver. Lancereaux[§] and Ogle[‖] have recorded cases of embolism at the bifurcation. In Lancereaux's case hepatic pain set in ten hours before death and was referred to the embolism. In Ogle's case there were anæmic infarcts in the liver, but no general necrosis of the liver. Necrosis of the liver has been recorded by Lancereaux and by Chiari in man, and experimentally embolism of the hepatic artery in the hands of Cohnheim and Litten,[**] and of Doyon and Dufourt,[††] has led to the same result. Short of this extreme result the flow of bile is retarded and infection of the bile-ducts rendered easier. In Lancereaux's cases of obstruction of the hepatic artery the liver became very greatly engorged from the absence of the driving power or *vis a tergo* normally supplied by the hepatic artery. In rare cases infarction of the liver may follow embolism. (*Vide* p. 104.)

Septic embolism of the small branches of the hepatic artery occurs in hæmic infections and gives rise to pyæmic abscesses. Embolism also occurs in generalized tuberculosis and sarcomatosis, especially in melanotic sarcoma.

THROMBOSIS.

This is also a pathological curiosity. Lancereaux[‡‡] describes a case of a clot in the trunk of an atheromatous hepatic artery in a man aged sixty-five who died with arteriosclerosis and gangrene of the feet which may have been either embolic or thrombotic.

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[*] Ross and Osler: Canadian Med. Journ., vol. vi.

[†] Kehr, H: München. med. Wochen., 1903, S. 1861.

[‡] Chiari: Zeitschrift f. Heilkunde, Bd. xix, S. 507.

[§] Lancereaux: Traité des Maladies du foie et du pancreas, p. 541.

[‖] Ogle, C.: Trans. Path. Soc., vol. xlvi, p. 72.

[**] Cohnheim and Litten: Virchow's Archiv, Bd. lxvii, S. 153.

[††] Doyon and Dufourt: Archiv de Physiol., 5th Series, vol. x, p. 522, 1898.

[‡‡] Lancereaux: Traité des Maladies du foie et du pancreas, 1899, p. 543.

ARTERIOSCLEROSIS.

The trunk of the hepatic artery is sometimes, in common with the rest of the arterial system, found to be atheromatous. When affected, the hepatic artery usually shows endarteritis deformans rather than endarteritis obliterans, or is dilated and varicose from loss of elasticity rather than narrowed. It thus disposes to the rare events, aneurysm and thrombosis of the hepatic artery. It is noticeable that arteriosclerosis does not lead to a fibrotic atrophy of the liver in any way resembling a granular arteriosclerotic kidney, though senile atrophy of the liver with some fibrous replacement might be thought to depend on a similar process. Inside the liver the branches of the hepatic artery show endarteritis in the neighbourhood of syphilitic gummata. In hæmochromatosis the hepatic artery shows endarteritis; occasionally in ordinary cirrhosis there is endarteritis obliterans. Bonome describes hæmorrhagic and necrotic infarcts due to endarteritis obliterans in cirrhosis. In general paralysis of the insane, which has been regarded by Bruce and by Ford Robertson as a chronic toxæmia of intestinal origin, Angiolella has observed endarteritis of the hepatic artery.

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Angiolella: Il Manicomio Moderno, 1894, 1895. Quoted by Robertson.
Bonome: Sperimentale, anno 53, fasc. 4. Quoted in Rev. Générale de Pathologie interne, 1900, p. 70.
Bruce: Brit. Med. Journ., 1901, vol. i., p. 1600.
Hasonfeld: Deutsch. Archiv f. klin. Med., 1897.
Robertson, Ford: Brit. Med. Journ., 1901, vol. i, p. 1602.

ENLARGEMENT OF THE HEPATIC ARTERY.

Enlargement of the hepatic artery is seen in cases of new-growth,—though not in all instances,—in cases of portal thrombosis of some standing, and in ordinary cirrhosis.

In a case where the liver weighed 14 pounds from carcinomatous infiltration, secondary to a primary growth in the œsophagus, the hepatic artery was dissected out and was small in size.

DISEASES OF THE HEPATIC VEINS.

Thrombosis; Stricture; Chronic Periphlebitis and Endophlebitis; Suppurative Phlebitis; Embolism.

THROMBOSIS.

Thrombosis of the hepatic veins is somewhat rare; it is usually a secondary effect of some other hepatic lesion, but may spread from the inferior vena cava. It may give rise to a nutmeggy condition of the liver and produce such stagnation and other changes that portal thrombosis results. It may be set up in the following ways:

(1) New-growth in the liver may extend into the hepatic veins and give rise to thrombosis.

(2) "Adenomata" in nodular hepatitis may rupture into the hepatic veins and thus lead to thrombosis.[*] The occurrence of such clots in the portal or hepatic veins, containing liver cells, has probably led some writers to consider that such cases of multiple adenomata in cirrhosis are carcinomatous, on the grounds that the growth has extended into the veins.

(3) In portal cirrhosis. Thrombosis of the hepatic veins is found in rare instances in cirrhotic livers. It may, as has just been pointed out, occur in cases of cirrhosis with multiple adenomata or nodular cirrhosis. Further, thrombosis of the hepatic veins may be due to intercurrent acute or subacute infections falling on a cirrhotic liver and setting up inflammation which involves the thin walls of the hepatic veins. It may be mentioned that in some cases, where thrombosis of the hepatic veins is associated with a slight degree of cirrhosis, the latter may be the result of thrombosis, being merely a secondary fibrous replacement.

(4) Thrombosis may be due to stricture and narrowing of the hepatic veins. Examples of this rare condition will be found on page 49, under the heading "Stricture." It is possible, as suggested by Fisher,[†] that the contraction of the veins is secondary to thrombosis and not the cause of it.

(5) Thrombosis may extend from the inferior vena cava.

I have seen a parietal thrombus in the inferior vena cava, where it grooves the liver, associated with thrombosis in the hepatic veins; there was more recent clot in the portal vein. In a case of obliteration of the inferior vena cava recorded by Reynaud the right hepatic vein was thrombosed. In a case of obliteration of the inferior vena cava recorded by Dixon Mann and Hall[‡] there were thrombi in the hepatic veins. In this case peritonitis was thought to have set up periphlebitis and endophlebitis and the subsequent changes in the inferior vena cava and hepatic veins.

[*] Compare Delépine: Trans. Path. Soc., vol. xli, p. 362.

[†] Fisher, T.: Bristol Medico-chirurg. Journ., vol. xx, p. 209.

[‡] Dixon Mann and W. Hall: Edinburgh Med. Journ., July, 1904, p. 57.

Osler * has described considerable stenosis of the orifices of the hepatic veins in a case of obliteration of the inferior vena cava, a condition which would readily dispose to thrombosis.

(6) Thrombosis of the hepatic veins may also occur in association with widespread venous thrombosis.

Pitt † records thrombosis in the aorta, in the splenic, left renal, and right middle cerebral arteries, and in the right hepatic vein. Softening and therefore older thrombi were found in the portal vein.

It appears probable that thrombosis of the hepatic veins may be due to the same causes that set up portal thrombosis, or to an extension of that process.

(7) It may not be possible to assign a definite cause for thrombosis of the hepatic veins in all cases. Possibly toxines or micro-organisms stopped by the liver may be responsible for some cases. Fisher ‡ reports a case of hepatic vein thrombosis in a child with bronchopneumonia. Thrombosis of the hepatic veins occurs as an early stage in suppurative inflammation due to hepatic abscess, pylephlebitis, etc.

Clinically thrombosis of the hepatic veins presents itself in much the same light as thrombosis of the portal vein; in fact, portal thrombosis may follow on hepatic vein thrombosis, as in the case mentioned on page 57. Ascites is generally present and may last for as long as four months; the liver may be palpably enlarged and gastro-intestinal hæmorrhages may occur. In cases of some standing the subcutaneous veins of the abdominal wall may be very greatly dilated. The *diagnosis* from portal thrombosis is very difficult; in both ascites may occur suddenly in a patient previously in good health. Ascites appears to be more rapidly fatal in thrombosis of the portal vein than in hepatic vein thrombosis. *Treatment* should be directed to any causal factor or associated condition likely to give rise to it, but as the diagnosis is seldom made, treatment is chiefly symptomatic.

STRICTURE OF THE HEPATIC VEINS.

Stricture of the hepatic veins chiefly occurs at or close to their junction with the inferior vena cava. Pressure from tumors, hydatid cysts, or cicatricial adhesions may obstruct branches of the hepatic veins in the liver and lead to local venous engorgement. (*Vide* Cardiac Liver.) Stenosis of the main trunks is rare. It may be due to the following causes:

(I) Cicatricial contraction starting outside the veins, either in the liver or in its neighbourhood. Under the name of phlebitis hepatica adhæsiva, Frerichs § described great narrowing of the hepatic veins due to inflammation spreading in from dense adhesions in the neighbourhood. His case was in an alcoholic married man aged forty-five; no mention of syphilis is made. He had ascites and jaundice; there were perihepatitis and probably some cirrhosis as well as a nutmeggy condition of the liver. Kelynack[*] met with a similar state of affairs in a woman aged thirty-two who had probably had syphilis. There were adhesions around the hepatic veins, with marked stenosis and thrombosis; the adhesions were thought to have produced the stenosis. When stenosis and thrombosis are associated, the stenosis is generally assumed to be primary; T. Fisher[†] suggests that in some cases the contraction of the veins may be the result of primary thrombosis.

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* Osler: Journ. Anat. and Phys., vol. xiii, p. 291.

† Pitt, G. N.: Trans. Path. Soc., vol. xlvi, p. 75.

‡ Fisher, T.: Loc. cit.

§ Frerichs: Diseases of Liver, vol. ii, pp. 432–437, New Sydenham Soc.

(II) To the effect of gummatous disease or syphilitic fibrosis in the immediate neighbourhood of the main hepatic veins. A gumma may be so situated as to lead to obliteration and thrombosis in one or both of the hepatic veins. Fagge[‡] refers to a case where one of the hepatic veins was so much narrowed by the pressure of a gumma that it only admitted a probe. In rare instances a gumma has been found involving the inferior vena cava and obliterating the openings of the hepatic veins. (Wilks,[§] West.[‖])

(III) To extensive hepatic fibrosis and cirrhosis. In some cases the cicatricial formation is very extensive and is associated with general hepatic fibrosis. There is not in all cases a certain syphilitic history, but there is sufficient evidence to suggest that congenital syphilis is a probable factor in the general and extensive fibrosis.

In a man aged twenty-six years under Dr. Churton's[**] care ascites suddenly set in, and death occurred nine days later from exhaustion. Very marked cirrhosis of the liver thought to be due to congenital syphilis with thrombosis and thickening of the walls of the hepatic veins was found at the autopsy; there was no portal thrombosis. A good example of cicatricial contraction involving and causing thrombosis of the hepatic veins was found in the body of a boy aged thirteen who died in St. George's Hospital with very marked cirrhosis of the liver. The patient had never taken alcohol, but there was reason to believe he was the subject of congenital syphilis, as his mother had three miscarriages after his birth and as there was marked fibrosis in the spleen, which weighed 16 ounces. The liver weighed 42 ounces and was considerably enlarged; it was most extensively fibrosed, and the large mass of cicatricial tissue involving the hepatic veins suggested early gummatous change; no caseation, however, could be seen microscopically.[††]

The following case is probably a combination of syphilitic cirrhosis with endophlebitis obliterans: Dr. Gee[‡‡] describes complete obliteration of the orifices of the hepatic veins in a child aged seventeen months. Ascites rapidly developed at the age of fourteen months, and paracentesis was twice performed. The liver weighed 16¾ ounces and was cirrhotic. There was considerable perihepatitis around the orifices of the hepatic veins. The hepatic veins ended abruptly, just short of entering the inferior vena cava, being cut off from it by a thin membrane only. The lining membrane of the vena cava where the mouths of the hepatic veins should have been showed dimples which had not at all the look of scars. Dr. Gee did not think this was congenital and due to a failure of union of the venæ revehentes hepaticæ with the inferior vena cava, for then the ductus venosus should have remained open. He regarded the primary change as cirrhosis which led to stenosis and obliteration of the hepatic veins. Some of the hepatic veins contained firm clot. The liver was nutmeg. There was a free collateral circulation especially

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[*] Kelynack: Med. Press and Circular, June 23, 1897.

[†] Fisher, T.: Bristol Medico-chirurg. Journ., vol. xx, p. 209, Sept., 1902.

[‡] Fagge: Principles and Practice of Medicine, vol. ii, p. 295, Ed. 1886.

[§] Wilks, S.: Trans. Path. Soc., vol. xiii, p. 123.

[‖] West, S.: Ibid., vol. xlii, p. 155. [**] Churton: Trans. Path. Soc., vol. l, p. 145.

[††] Lazarus-Barlow, W. S.: Path. Trans., vol. l, p. 147. St. George's Hosp. Museum, Ser. ix, 174 L.

[‡‡] Gee: St. Bartholomew's Hospital Reports, vol. vii, p. 144, 1871.

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around the left branch of the portal vein. Similar cases have been described by Rosenblatt,* and Penkert.†

(IV) To primary obliterative endophlebitis of the hepatic veins. In a few cases there is marked or almost complete stenosis of the openings of the hepatic veins into the inferior vena cava without any evidence that the inflammatory process has spread to the veins from adjacent parts. Craven Moore ‡ has collected 12 cases of this primary obliterative inflammation of the hepatic veins. The openings into the inferior vena cava may be mere dimples.

In some instances, as in Chiari's § three cases, syphilis was regarded as responsible, but there is no reason to think that this holds good in all cases. The entrance of the ductus venosus into the inferior vena cava in the immediate neighbourhood of the hepatic veins suggests that the process of obliteration of that fœtal vessel may spread to the orifices of the hepatic veins and, by excess of the obliterating process, gradually lead to stenosis of the orifices of the hepatic veins, just in the same way that stricture of the ileum sometimes occurs at the point where Meckel's diverticulum is normally obliterated. A more closely analogous case is to be found in the stenosis (or coarctation) of the aorta at the point where the ductus arteriosus joins the aorta; this process slowly progresses and eventually leads to extreme narrowing or even complete obliteration of the lumen of the aorta. It seems reasonable to imagine that a similar train of results may follow obliteration of the ductus venosus. Moore, however, believes that congenital influences may so reduce the resistance of the mouths of the hepatic veins as to enable some hæmatogenous poison to induce endophlebitis.

The liver is in a state of advanced chronic venous engorgement with dilatation of the trunks of the hepatic veins behind the stenosis. Secondary thrombosis is frequent.

Symptoms.—The symptoms are practically the same as those referred to in the section on Thrombosis of the Hepatic Veins. Ascites is almost constant, hæmatemesis rare, and jaundice exceptional. The average age, according to Craven Moore, is about twenty-nine years, and the sexes are equally affected.

CHRONIC PERIPHLEBITIS AND ENDOPHLEBITIS OF THE HEPATIC VEINS.

Spread of inflammation around the inferior vena cava to the hepatic veins in adherent pericardium may result in periphlebitis and possibly slight fibrosis in the neighbourhood. In the cases that I have examined, however, there has been no extension of inflammation from the walls of the veins into the surrounding liver substance. In long-standing backward pressure the intima of the hepatic veins may, like that of the inferior vena cava, become somewhat thickened and opaque—a slight degree of chronic endophlebitis due to increased intravascular pressure, and the veins become dilated. Endophlebitis may spread from the inferior vena cava in cases of obliteration of that vessel into the hepatic veins, and may, as in Dixon Mann and Hall's* case, give rise to thrombosis of the hepatic veins.

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* Rosenblatt: Virchow's Jahresbericht, 1867, Bd. i, S. 226.

† Penkert: Virchow's Archiv, Bd. clxix.

‡ Craven Moore's (Medical Chronicle, July, 1902) cases were those of Frerichs, (2), Gee, Rosenblatt, Schuppel, Hainske (2), Chiari (3), Leichtenstern, and his own. Some of these cases have been referred to under other causes of stenosis of the hepatic veins.

§ Chiari: Beiträge z. path. Anat. u. z. allg. Path., Bd. xxvi.

SUPPURATIVE PHLEBITIS OF THE HEPATIC VEINS.

Suppurative phlebitis is more likely to attack the hepatic veins than the branches of the portal vein in hepatic abscess, since the latter are surrounded by Glisson's capsule, while the hepatic veins and their branches are not protected in this way. When the hepatic veins are thus affected, general pyæmia is more likely to occur than in pylephlebitis, since the emboli can pass more readily into the circulation.

In a case of large hepatic abscess in a man aged thirty-four the abscess set up thrombosis in the right hepatic vein which produced embolism of the right pulmonary artery and suppurating areas in both lungs. In a case of suppuration around a calculous gall-bladder recorded by West † the abscess opened into the hepatic veins and produced multiple infarcts in the lungs.

In a case of proctitis, due to a bacillus of the influenza group, Ophüls ‡ found abscesses in the submucous coat of the rectum, areas of necrosis in the liver, and suppurative thrombosis of the hepatic veins which had produced secondary foci in the right lung. The portal vein was quite healthy.

EMBOLISM OF THE HEPATIC VEINS.

Embolism of the hepatic veins can occur only when the embolus travels against the blood-stream and enters the hepatic veins from the inferior vena cava—in other words, in retrograde embolism. Retrograde embolism of veins is very rare; when it occurs, it is more frequently seen in the hepatic veins, since they are not protected by valves, and are so close to the heart that fragments of growth or thrombus may drop into their orifices either from the inferior vena cava or from the heart and superior vena cava. Welch § in his article on embolism quotes examples of fragments of new-growth being found in the hepatic veins in cases where the primary growths were in the abdomen and thyroid gland.

It seems probable that in cases of cranial suppuration with secondary abscesses in the liver, without any abscesses in the lungs, the micro-organisms may drop down the jugular vein, superior vena cava, right auricle, and inferior vena cava into the orifices of the hepatic veins, and so infect the liver. The production of retrograde embolism probably depends on the temporary stagnation or reversal of the direction of the blood-flow. Thus if a thrombus was passing up the inferior cava and a violent expiratory effort or cough occurred at the moment when it was opposite the openings of the hepatic veins, the embolus might be carried into the liver.

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* Dixon Mann and W. Hall: Edinburgh Med. Journ., July, 1904, p 57.

† West, S.: Path. Trans., vol. xxxvii, p. 281.

‡ Ophüls: American Journ. of Med. Sciences, 1901, p. 797.

§ Welch, W. H.: Allbutt's System of Medicine, vol. vi, p. 232.

THROMBOSIS OF THE PORTAL VEIN.

Synonyms: Pylethrombosis, Pylephlebitis Adhæsiva.

In this condition there is thrombosis of the portal vein which does not go on to suppuration.

CAUSATION.

In considering the causes of thrombosis of the portal vein it will be convenient to deal first with thrombosis depending upon inflammatory and other morbid conditions of the portal vein, and then to consider the influence of hepatic cirrhosis, intra-abdominal malignant disease, tumors, adhesions, and traumatism, in the production of portal thrombosis.

Inflammatory Conditions Causing Portal Thrombosis.—Thrombosis of the portal vein, or, as it may in this particular connexion be more appropriately called, adhesive pylephlebitis, occurs as a preliminary stage in the course of suppurative pylephlebitis. By extension from adjacent parts inflammation may spread to the walls of the portal vein and set up thrombosis which does not necessarily go on to suppuration. This may occur in cholangitis, in pancreatitis, in peripancreatitis, in hepatic and subphrenic abscesses, and in other conditions. As a good example of portal thrombosis in an early stage of suppurative pylephlebitis Rose Bradford's * case may be quoted:

A man aged twenty died from intestinal obstruction due to suppurative phlebitis of the superior mesenteric vein regarded as secondary to suppuration in a mesenteric gland. The portal vein was blocked by recent clot.

Cholelithiasis, by setting up cholangitis and pericholangitis, may lead to inflammation of the walls of the portal vein and subsequently to thrombosis.

A good example of this is given by Rabé: † In a man aged seventy-three who died with ascites, a calculus was found impacted in the duodenal end of the bile-duct, causing dilatation of the duct behind this point; around the bile-duct there was fibrosis which involved the portal vein. The walls of the vein were thickened and contained firm clot.

Extension of inflammation from an hepatic abscess is a rare cause of thrombophlebitis of the portal vein; the hepatic veins, being unprotected by the sheath of Glisson's capsule, are more likely to be affected.

A man aged twenty-seven, who had contracted dysentery in the Boer War of 1899–1902, was brought in a moribund state into St. George's Hospital. At the autopsy there was acute peritonitis and several pints of turbid fluid in the abdominal cavity, due to rupture of an abscess in the left lobe of the liver into the peritoneal cavity. There was a firm dry clot in the portal vein, which might have given rise to the ascites. The walls of the portal vein were greatly thickened and the lymphatic glands in the portal fissure much enlarged. It seemed probable that the infection had spread, at any rate partly, by the lymphatic vessels from the abscess to the trunk of the portal vein.

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* Bradford, J. R.: Trans. Clinic. Soc., vol. xxxi, p. 203.

† Rabé: Bull. Soc. Anat. Paris, 1898, p. 170.

Inflammation, abscess, or infarction of the spleen may set up thrombosis of the splenic vein, which by extension may spread into the portal vein.

Simple ulcer of the stomach must be a very rare cause of portal thrombosis. Wickham Legg * mentions two cases; but I have no other references. In this connexion it may be pointed out that thrombosis of the gastric veins may cause ulceration of the gastric mucous membrane. I have seen this in a case where suppurative pylephlebitis was due to appendicitis. Indirectly a gastric ulcer may cause portal thrombosis by giving rise to a localized abscess in the neighbourhood. I have seen portal thrombosis in a case of subphrenic abscess due to perforation of a gastric ulcer.

Probably in many of the cases that appear to be primary thrombosis there is in reality microbic infection of a low grade of virulence present which is responsible for the production of a thrombus. The term "adhesive pylephlebitis," formerly used to designate thrombosis of the portal vein, is an expression of the view originated by Hunter and Cruveilhier that thrombosis was always the result of phlebitis. Bacteriological examination † shows that many thrombi which would formerly have been regarded as marantic contain micro-organisms, and though the presence of micro-organisms does not necessarily prove that they played a causal part in the production of thrombosis, it justifies the tendency to return to the point of view of Hunter that most thromboses are secondary to infection of the wall of the vein.

Disease of the Portal Vein.—*Chronic phlebosclerosis*, which is probably often due to increased blood-pressure in the portal vein, plays an important part in producing portal thrombosis. Though generally associated with cirrhosis, chronic portal phlebitis may occur independently of any hepatic disease. It is quite possible that similar changes in the vein wall may result after thrombosis has taken place; but it seems probable that phlebosclerosis usually precedes and disposes to portal thrombosis.

Borrmann,‡ who has insisted on this sequence of events, found phlebosclerosis in 7 out of 20 cases of portal thrombosis.

When the change is of old standing, calcification of the wall of the vein may occur and calcareous plates or spicules may project into the lumen of the portal vein and induce thrombosis.

In a patient of Dr. Ewart's, on whom I made a postmortem examination at St. George's Hospital, the dependence of thrombosis on calcification of the wall of the portal vein seemed clear. A man aged sixty-six years, addicted to some alcoholic excess, had been in good health until two months before his death, when ascites appeared. He was thin, but there had been no melæna or hæmatemesis. Paracentesis was required, but the fluid reaccumulated, diarrhœa set in, and he became delirious and finally died comatose. At the autopsy there were pigmented scars in the colon as if from old dysentery, but no ulceration. There was localized fibrinous peritonitis around the site of the trocar punctures. The portal vein was much thickened and showed calcification, and there was a softening thrombus in the right branch of the portal vein. The splenic vein was occluded at its entry into the portal vein and contained a crumbling thrombus in contact with an area of calcification in its wall. The thrombosis did not correspond to the more extensive changes in the walls of the portal vein, and it therefore appeared probable that the thrombosis was secondary to the changes in the portal vein, as presumably the thrombosis had only existed since the ascites developed, viz., two months. The liver was atrophied, weighing 32 ounces, but not cirrhotic. The spleen weighed 18 ounces and on section appeared fibrotic, but did not present any infarcts.

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* Legg, Wickham: St. Bartholomew's Hosp. Reports, vol. x, p. 236.

† Vaquez: Thèse de Paris, 1890. Bryant, J. H.: Guy's Hosp. Reports, vol. lvi, p. 99.

‡ Borrmann: Deutsch. Archiv f. klin. Med., Dec. 9, 1897.

Syphilitic inflammation of the portal vein may probably give rise to thrombosis in some cases. This may occur in both the hereditary and the acquired form of the disease, but more exact knowledge is required on this point.

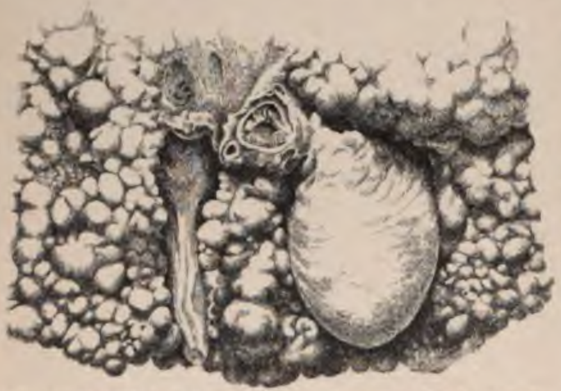

FIG. 10.—THE UNDER SURFACE OF A CIRRHOTIC LIVER, SHOWING THROMBOSIS OF THE PORTAL VEIN. (Drawn by Dr. E. A. Wilson.)

Cirrhosis of the Liver.—Thrombosis of the portal vein is most often found to be associated with portal cirrhosis. Fagge,* indeed, stated that he had only met with it in that disease or in association with perihepatitis. Although cirrhosis is the most frequent cause of portal thrombosis it does not appear to be present in half the total cases of that condition.

In 60 cases collected from various sources, including most of Langdon Brown's, there were 22, or 36.6 per cent., due to cirrhosis. These 22 cases do not include cases where cirrhosis and intra-abdominal malignant disease were both present, or those few cases where the observers believed cirrhosis to be secondary to portal thrombosis.

Portal thrombosis is far from common in cirrhosis of the liver.

In a period of thirty-three years Langdon Brown † found that in 334 autopsies performed on cases of hepatic cirrhosis at St. Bartholomew's Hospital 10, or 3.3 per cent., were complicated by thrombosis of the portal vein.

In cirrhosis of the liver there are a number of factors favouring portal thrombosis. There are obstruction to the passage of blood through the liver and stagnation of blood in the vein, while the increased venous pressure tends to set up endophlebitis and even secondary calcification of the walls of the vein. Further, the catarrhal condition of the intestinal tract, so common in portal cirrhosis, favours microbic invasion of the walls of the tributaries of the portal vein. In cases of nodular cirrhosis, or cirrhosis with multiple adenomata, thrombosis of the portal vein is relatively common; thus, in fifteen cases collected by Ll Powell * there was portal thrombosis in nine. The contents of the "adenomata" may soften down from necrosis and discharge into the portal vein, thus setting up thrombosis. On the other hand, thrombosis of the portal vein may so impair the nutrition of the "adenomata" as to set up fatty degeneration and necrosis.

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* H. Fagge: Principles and Practice of Medicine, Ed., 1886, vol. ii, p. 297.

† Langdon Brown: St. Bartholomew's Hospital Reports, vol. xxxvii, p.62.

Intra-abdominal Malignant Disease.—After cirrhosis the commonest condition associated with portal thrombosis is malignant disease either in the liver itself or elsewhere in the abdominal cavity. In sixty cases of portal thrombosis ten were associated with some form of intra-abdominal malignant disease.

Malignant Disease of the Liver.—Carcinoma of the liver may eat its way into the branches of the portal vein and induce thrombosis; this may occur either in primary or secondary malignant disease of the organ, but it is particularly prone to occur when primary carcinoma supervenes in a liver which is already cirrhotic. In these cases the contents of the portal vein may be composed of growth as well as of blood-clot. It is only a step from cirrhosis with adenoma to carcinoma with cirrhosis, and it is difficult to be certain in many of the published cases whether the growth was still adenomatous or had become malignant. The two conditions further show their close resemblance by the frequency with which portal thrombosis occurs in both.

In other forms of intra-abdominal disease, such as carcinoma of the stomach, pancreas, colon, etc., the growth may involve the tributaries of the portal vein, spread along them, and set up secondary thrombosis.

Carcinoma of the Stomach.—Malignant disease of the stomach occasionally gives rise to portal thrombosis. S. and S. Fenwick † found this complication in 3 per cent. of their cases of gastric carcinoma and consider that this is probably understating the incidence. Gastric cancer may set up portal thrombosis in several ways; the growth may enter the gastric veins and extend directly into the portal vein and set up secondary thrombosis, pass up the lesser omentum by continuity and compress and involve the portal vein, or by means of secondary growths in the portal fissure or in the substance of the liver may compress the portal vein.

In the following case there were at least two factors favouring thrombosis of the portal vein. A woman aged sixty-five years died in St. George's Hospital with a small cirrhotic liver weighing 28 ounces and a spheroidal celled carcinoma near the pylorus. The trunk of the portal vein was thickened and surrounded by adhesions. The right branch of the portal vein was thrombosed and there was an adherent clot at the entrance of the splenic vein.

In a case of portal thrombosis secondary to gastric carcinoma Longcope ‡ found infarcts in the liver.

Pressure on the portal vein, by tumors, adhesions, and altered conditions of adjacent viscera, may be, but is not necessarily, accompanied by thrombosis of the portal vein. By pressure the nutrition of the walls of the vein is impaired, microbic infection is thus favoured, and stagnation of the blood is induced—factors which all dispose to thrombosis. Pressure may be exerted on the portal vein in a number of ways, chiefly by malignant disease involving the adjacent lymphatic glands or the head of the pancreas.

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* Ll Powell: Unpublished Thesis for M. B. degree, Cambridge, 1895.

† Cancer and Other Tumours of the Stomach, p. 72.

‡ Longcope: University of Pennsylvania Med. Bull., Aug., 1901, p. 223.

Malignant Disease of the Pancreas.—In 41 cases of portal thrombosis Langdon Brown found that the condition was associated with malignant disease of the pancreas in three instances. Sometimes when a malignant growth, which compresses the portal vein, also infiltrates its walls, a finger-like process of the growth may extend along the lumen of the vein and then set up a secondary thrombosis. This very rarely happens in malignant disease of the pancreas; it is chiefly seen in malignant disease in the liver.

Malignant disease of the glands in the portal fissure secondary to malignant disease of the stomach, pancreas, liver, or gall-bladder might compress the portal vein. Malignant disease of the liver may compress as well as invade branches of the portal vein, and set up thrombosis which travels distally into the main trunk. Portal thrombosis has been recorded in primary carcinoma of the bile-ducts. (Bourgeret and Cossy.*)

Chronic Pancreatitis.—The cicatricial contraction of chronic inflammation of the head of the pancreas may greatly constrict the superior mesenteric vein and lead to thrombosis which eventually extends into the portal vein. Barnard † met with a case of this kind. Probably many cases of chronic pancreatitis were formerly spoken of as "scirrhus" of the pancreas.

The traction exerted by adhesions due to gastric or duodenal ulcers (Frerichs ‡) may compress the portal vein and in rare instances induce thrombosis. Similarly inflammatory adhesions involving the mesenteric veins may start thrombosis which may extend upwards into the trunk of the portal vein. Cases recorded by F. Taylor § and R. Johnson ‖ illustrate the production of portal thrombosis in this way.

Chronic peritonitis in rare instances may be the only other morbid lesion forthcoming, and so appear to be the cause, either by extension of inflammation to the walls of the portal vein, or, in very rare instances, by constricting or compressing the vein.

In St. Bartholomew's Hospital Museum there is a specimen [No. 2205 A] of thrombosis associated with chronic peritonitis; the liver was not cirrhotic. Frerichs quotes some similar cases.

The mechanical pressure exerted by a calculus in the gall-bladder, or more frequently in the ducts, on the portal vein may give rise to simple thrombosis. This is more likely to occur when the calculus is in the common duct, where it is in close contact with the portal vein.

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* Bourgeret and Cossy: Bull. Soc. Anat. Paris, 1873, p. 347.

† Barnard, H. L.: *Vide* Langdon Brown, St. Bartholomew's Hosp. Reports, vol. xxxvii, p. 87.

‡ Frerichs: Diseases of the Liver, vol. i, p. 1172.

§ Taylor, F.: Trans. Path. Soc., vol. xxxii, p. 21

‖ Johnson, R.: Trans. Clinic. Soc., vol. xxxi, p. 212.

Cases are recorded by Leudet, Geigel, Naunyn,[*] Westenhöffer,[†] Körte.[‡] Naunyn also describes a case where a calculus in the cystic duct compressed and gave rise to portal thrombosis, and refers to a case of Klesser's where a calculus in the same position compressed one branch of the portal vein. Donkin[§] met with portal thrombosis due to pressure exerted by several calculi in the gall-bladder on the vein.

Gummatous inflammation in the portal fissure is a rare cause of thrombosis of the portal vein. It is possible that *aneurysm* of the abdominal aorta or of the hepatic artery may press on the portal vein and induce thrombosis.

Traumatism may be followed by portal thrombosis. Welch[‖] mentions a case where symptoms strongly suggesting pylethrombosis followed a blow on the abdomen; but recovery took place. Pitt[**] described a man who after a fall on his side vomited and became collapsed; he was found to have a strangulated scrotal hernia; at the operation the bowel was found to be bruised. Death occurred five days later and thrombosis of one of the intrahepatic branches of the portal vein was found. As an example of post-operative thrombosis Delatour's[††] case of thrombosis of the splenic vein after splenectomy, extending into the portal vein, may be mentioned. Traumatism involved in volvulus or in kinking of the mesentery may be the starting-point of thrombosis in the portal area. Langdon Brown refers to an example of this kind.

Thrombosis of the portal vein may be secondary to *thrombosis of the hepatic veins.*

At the post-mortem examination of a woman aged fifty-two who died in St. George's Hospital in 1898 there was marked ascites with very little chronic peritonitis. The intestines were full of blood and deeply congested; no enlargement of the cutaneous veins over the abdomen or of those of the œsophagus or retroperitoneal space. The inferior vena cava showed a decolorised parietal clot close to the opening of the hepatic veins; the right hepatic vein was blocked with decolorised clot; the left was normal. The inferior vena cava was not obstructed and there was no clot elsewhere in its course. The portal and splenic veins were blocked by more recent clot. The liver was much atrophied, markedly nutmeg, and somewhat fatty, but not cirrhotic to the naked eye. Microscopically there was extensive atrophy of the liver cells, but they were not necrosed or destroyed as they are in acute yellow atrophy. The fibrous tissue around the portal spaces was prominent from the atrophy of the liver cells, but there was no definite evidence of cirrhosis. The spleen weighed 9 ounces. There were numerous cutaneous and visceral hæmorrhages.[‡‡]

Puerperal eclampsia has been thought by Schmorl[§§] to induce portal thrombosis. This may be the result of degenerative changes in the liver giving rise to discharge of necrotic hepatic cells and tissue fibrinogens into the portal vein.

In a number of cases there is no local cause or associated morbid change, such as cirrhosis or inflammation, to account for portal thrombosis. In some of these cases it is associated with thrombosis elsewhere in the body, and therefore almost certainly depends on a widespread change in the blood of either a chemical or infective nature. It is analogous to the thrombosis sometimes seen in marasmus and in anæmias. The altered blood condition must favour infection, and the intestinal tract would appear to be so eminently favourable to the passage of micro-organisms into the tributaries of the portal vein that it is surprising that portal thrombosis is so comparatively infrequent. I have myself on two occasions seen portal thrombosis associated with thrombosis in the iliac veins. Langdon Brown found that in 33 cases 6 were associated with thrombosis elsewhere.

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[*] Naunyn: Cholelithiasis, p. 133.

[†] Westenhöffer: La Semaine Médicale, 1903, p. 32.

[‡] Körte: Ibid.

[§] Donkin: Medical Press and Circular, 1868, vol. ii, p. 396.

[‖] Welch, W. H.: Allbutt's System, vol. vi, p. 220.

[**] Pitt, G. N.: Trans. Path. Soc., vol. xlvi, p. 74.

[††] Delatour: Annals of Surgery, vol. xxi, p. 24.

[‡‡] Rolleston: Trans. Path. Soc., vol. l, p. 148.

[§§] Schmorl: Quoted by Welch, Allbutt's System, vol. vi, p. 219.

It is curious that nothing is known as to the occurrence of portal thrombosis in connexion with diseases such as gout, influenza, pneumonia, typhoid fever, etc., which lead to thrombosis elsewhere in the body. It is specially noticeable that thrombophlebitis of the portal vein does not occur in or after enteric fever.

Sex.—More cases occur in males than in females. In 62 cases, 38 were males and 24 females; the preponderance of males depends on the greater frequency of hepatic cirrhosis in that sex. Cirrhosis of the liver was present in 18 out of the 38 males and in only 4 of the 24 female cases. Intra-abdominal malignant disease accounted for 8, or exactly one-third of the cases of portal thrombosis in women.

Age.—In 61 cases the average age was forty-four years. The extremes were eighty years in a man and five years in a girl.* In the two sexes the average ages were 44.8 years among the males and 41 years among the females. This again corresponds with the slightly earlier age at which cirrhosis is fatal in women. There were ten patients under thirty years of age, equally divided among the two sexes; four were under twenty years of age—three females and one male. The average age of portal thrombosis is thus more than twelve years above the average age [31.6 years] in suppurative pylephlebitis. The explanation of this is to be found in the fact that the two conditions—hepatic cirrhosis and intra-abdominal malignant disease—which most frequently cause portal thrombosis are commoner after forty years of age, while appendicitis, which is the most prolific source of suppurative pylephlebitis, is essentially a disease of young persons.

DISTRIBUTION OF THE THROMBOSIS ON THE PORTAL VEIN.

The thrombosis varies considerably in its distribution. It may be extensive and spread throughout the portal vein, its tributaries and branches. Usually it is more limited; it may occupy the main trunk of the portal vein and one or both of its branches in the liver, or it may obstruct the trunk and one or more of its tributaries, while in other instances thrombosis may be confined to one of its intra-hepatic branches or one of its tributaries. The clot obstructing a tributary, such as the splenic vein, may just project into, but not obstruct, the blood-flow through the main trunk of the portal vein; in many instances the clot extends from the tributaries upwards into the portal vein. In other instances the clotting may begin in the portal vein and subsequently spread into the peripheral tributaries. Thrombosis may be confined entirely to the tributaries of the portal vein—the splenic, superior and inferior mesenteric veins—or to its intra-hepatic branches. Though this can hardly be called portal thrombosis, it is difficult to separate thrombosis of the main trunk of the portal vein from thrombosis of its branches.

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* Taylor, F.: Trans. Path. Soc., vol. xxxii, p. 61.

MORBID ANATOMY.

The thrombosed vein is distended with clot, and thus differs from the more or less collapsed condition of the portal vein when containing ordinary post-mortem blood-clot. Distal to the obstructing thrombus the vein may be considerably dilated or even sacculated; this may also occur in the splenic vein. The vein wall is usually thickened, sometimes considerably so, from chronic phlebosclerosis, a condition analogous to arteriosclerosis, which Borrmann considers may be responsible for thrombosis. The wall of the vein sometimes contains calcareous plates, a further stage of chronic phlebosclerosis. In other instances the vein wall is swollen from recent inflammation. In cases where the patient lives for a long time after the onset of thrombosis the portal vein may be reduced to a mere cord of fibrous tissue. In such cases a collateral circulation is developed and quite a plexus of veins may be found in the position of the portal vein. It is very possible that in some cases thickening and calcification of the walls of the portal vein are results of thrombosis with partial canalization and organization of the blood-clot.

The character of the clot varies according to its age: it may be quite recent and not very firmly adherent to the vein wall, or it may be granular, decolorized, or even laminated. In some instances the lumen of the vein is not obliterated, the clot being only parietal. As has already been mentioned, the thrombosis may be parietal in one part of the portal vein and completely obstruct the lumen in another, or the central part of the clot may be canalized. When the central part of the thrombus softens down, the condition approaches, if it does not merge into, suppurative pylephlebitis. The thrombus may obstruct, without spreading into, the orifice of one of the tributaries of the portal vein; this is not uncommon at the junction of the splenic vein with the trunk of the portal vein.

The Liver.—The liver may present conditions that have caused or favoured the occurrence of thrombosis in the portal vein, such as portal cirrhosis, nodular cirrhosis, primary or secondary malignant disease, or abscess. The liver may show changes depending on and secondary to portal thrombosis. Thus, the hepatic artery may be enlarged in order to compensate for obstruction to the advent of blood to the liver by means of the portal vein. Thrombosis of the portal vein may be associated with a fatty and necrotic condition of the "hobnails" of a cirrhotic liver, and it may reasonably be believed that portal thrombosis, by cutting off the blood-supply, has brought about this change. It is, however, possible that the converse occurs, and that a softened hobnail may, by discharging into a branch of the portal vein, start thrombosis.

Infarcts, though rare in the liver, are, when present, associated in a fair percentage of the cases with portal thrombosis. They are, however, very far from being a necessary sequence of that condition. Some other factor, such as obstruction of the hepatic artery or a toxic condition of the blood, is necessary before infarction occurs in portal thrombosis. (*Vide* page 104.) The softening and necrosis of cirrhotic hobnails in portal thrombosis might be compared with the production of an anæmic infarct in an otherwise healthy liver under similar conditions. In portal thrombosis the infarcts are usually red or hæmorrhagic, and in only a few instances anæmic.

Frerichs[*] describes local atrophy and depressions, sometimes leading to a lobulated condition of the liver, as a result of obstruction of individual branches of the portal vein. It is possible that in an early stage of these cases of atrophy there was an infarct.

In some cases where the portal vein has been thrombosed for some considerable time the liver may show very little change, or may merely be fatty.

In a remarkable case recorded by Langdon Brown[†] symptoms of portal obstruction had existed for twenty years, and indeed this diagnosis had been made early in the patient's illness by the late Sir William Jenner. The portal vein was represented by a fibrous cord with a minute lumen. The liver was described as natural though pale. In a case of much the same kind recorded by Cruveilhier[‡] the liver was unaltered. In other instances the liver is small, atrophied, and shows a little replacement fibrosis. In a case regarded as primary thrombosis of the portal vein by Dickinson[§] in a woman aged twenty-one, the liver, though fatty, presented no signs of cirrhosis and weighed only 28 ounces. A similar case was recorded by Peacock.[‖] In a case under Dr. Penrose's care, which I examined after death, the liver weighed 46 ounces and appeared atrophied to the naked eye. Microscopically there was no evidence of cirrhosis, though the fibrous tissue around the portal areas was very prominent. I have found exactly the same appearances in two other cases examined postmortem and microscopically.

It has been thought by West[**] and Goodhart[††] that thrombosis of the portal vein may give rise to portal cirrhosis in a previously healthy liver. There is ample evidence that this need not occur; on the other hand, some atrophy of the liver cells with fibrous replacement is not uncommon, and this relative fibrous increase might have been regarded as cirrhosis of slight degree.

Fibrosis of the liver was produced in dogs by Solowieff[‡‡] as a result of gradual thrombosis of the portal vein. This might possibly have been due to some extension of inflammation into the liver along the portal vein, or have been a replacement fibrosis associated with atrophy of the liver cells from diminished blood-supply.

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[*] Frerichs: Diseases of the Liver, vol. ii, p. 396. Translated by New Sydenham Soc.

[†] Langdon Brown: St. Bartholomew's Hospital Reports, vol. xxxvii, p. 64.

[‡] Cruveilhier: Atlas d'Anat. Pathol., livraison xvi, Pl. 6.

[§] Dickinson: Trans. Path. Soc., vol. xiv, p. 63.

[‖] Peacock: Trans. Path. Soc., vol. xxiv, p. 122.

[**] West, S.: Trans. Path. Soc., vol. xxix, p. 106.

[††] Goodhart: Trans. Path. Soc., vol. xl, p. 134.

[‡‡] Solowieff: Virchow's Archiv, Bd. lxii. S. 195, 1875.

Bermant's * experimental researches support Solowieff's views as to cirrhosis being produced by portal obstruction, while Cohnheim and Litten † came to a diametrically opposite conclusion.

To sum up the late effects of portal thrombosis on the liver, there may be no alteration except slight fatty change; there may be atrophy of the liver with some fibrous replacement, but there is very little reason to believe that genuine cirrhosis is produced in this way.

Spleen.—Enlargement of the spleen is almost constant when the trunk of the portal vein is completely occluded by a thrombus. Langdon Brown estimates that it is enlarged in 70 per cent. of the cases. Enlargement may be reduced by copious ascites or gastro-intestinal hæmorrhages or prevented by firm perisplenic adhesions or chronic capsulitis.

In a case under my care of thrombosis of the portal vein in cirrhosis associated with rapid and excessive ascites the spleen only weighed 4 ounces.

On the other hand, there may be no splenic enlargement with a parietal thrombosis of the portal vein or where the mesenteric veins only are obstructed. Very great enlargement of the spleen follows complete thrombosis of the splenic vein; it may weigh 20 or 30 ounces and may show infarcts,‡ either anæmic or hæmorrhagic. In connection with the association of infarcts and thrombosis of the splenic vein it should be remembered that an infarct due to arterial embolism may induce thrombosis, possibly by the liberation of tissue fibrinogens.

Intestines.—When there is extensive thrombosis of the mesenteric veins there may be hæmorrhagic infarction going on to gangrene in part of the small intestine, usually in the middle of the jejunum. The fact that the middle of the jejunum is more often affected than the rest of the intestine is due to this part of the bowel being entirely dependent for its blood-supply on the superior mesenteric artery and unable to draw any blood from other sources, such as the parietal veins around the duodenum and cæcum.§ A good example of hæmorrhagic infarction of 9 inches of the jejunum due to this cause is in St. Bartholomew's Hospital Museum (1956 g).

I have seen secondary ulceration of the stomach occur from portal thrombosis. When the portal vein has been obstructed for some considerable time, the small veins in the intestines, or more rarely in the stomach, may be considerably dilated. A varicose vein in the stomach may become eroded and give rise to fatal hæmorrhage.

CLINICAL PICTURE.

Onset.—In the presence of cirrhosis of the liver or intra-abdominal disease there may be nothing to mark the occurrence of portal thrombosis, especially when ascites is already present. In latent cirrhosis or other cases where the patient has been in good or in fair health the onset may be sudden and marked by the rapid development of ascites or by profuse hæmatemesis. In 34 cases analyzed by Langdon Brown the onset was gradual in 14 and acute in 20.

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* Bermant (1897): Quoted by Welch, Allbutt's System, vol. vi, p. 221.

† Cohnheim and Litten: Virchow's Archiv, Bd. lxvii, S. 153, 1876.

‡ Rolleston: Trans. Path. Soc., vol. xliii, p. 49.

§ Barth: Soc. méd. des Hôp. Paris, Oct. 28, 1897.

Symptoms and Signs.—The clinical manifestations of portal thrombosis present a certain amount of variation which may roughly be correlated with the situation and extent of the thrombosis in the portal area. Thus, if the portal vein alone is involved, the most prominent symptom is that of obstruction to the passage of blood through the liver, viz., ascites, while hæmatemesis may also occur. If the thrombus occludes the proximal end of the splenic vein where it joins the portal vein, enlargement of the spleen and hæmatemesis may be expected. Thrombosis of the mesenteric veins is associated with intestinal obstruction, diarrhœa, melæna, and collapse.

Arranged in the order of their frequency and importance, the chief clinical features of portal thrombosis are: ascites, enlargement of the spleen, gastro-intestinal hæmorrhages, abdominal pain, symptoms of intestinal obstruction, diarrhœa, and manifestations of toxæmia resembling those in the late stages of cirrhosis, and not unlike uræmia. It will be seen that thrombosis of the portal vein may present the aspect of cirrhosis of the liver, of a gastro-intestinal disorder, or may combine the features of these two groups.

Ascites is the most frequent clinical manifestation. In 61 collected cases it was present in 40, or 65.6 per cent. It may be absent in acute cases where death rapidly results from gastro-intestinal hæmorrhage, or where the mesenteric veins are chiefly involved and the symptoms suggest intestinal obstruction. Copious gastro-intestinal hæmorrhage or diarrhœa may prevent the development of ascites. In the rare cases where life has been prolonged for years there may be no ascites, presumably from compensation brought about by a free collateral anastomosis. Stress was laid by Frerichs on the rapid development of ascites and on its reaccumulating directly after paracentesis as an important diagnostic sign of portal thrombosis, but it must be admitted that this is not of much value, inasmuch as the same phenomena may occur in cirrhosis and occasionally in ascites due to other causes, *e. g.*, tuberculous peritonitis.

Enlargement of the Spleen.—The spleen is very frequently found enlarged after death, but is not palpable in all these cases during life. Since most statistics refer to the size of the spleen as determined after death, a much lower estimate than 70 per cent., the percentage arrived at by Langdon Brown by adding his 41 cases to Frerichs' and to 25 collected by Crofton-Atkins, must be made of the existence of a palpable spleen *intra vitam*. The enlargement may be masked by ascitic or tympanitic distension of the abdomen. Enlargement may be observed to diminish after copious gastro-intestinal hæmorrhage. Very considerable enlargement should suggest the possibility of hæmatemesis or melæna due to a thrombus obstructing either the splenic vein or its junction with the portal vein.

Gastro-intestinal symptoms are somewhat variable and are related to thrombosis involving the trunks or orifices of the gastric and mesenteric veins, rather than to thrombosis of the trunk of the portal vein in the hilum of the liver. Gastro-intestinal hæmorrhage was noted in 27 out of 61 collected cases, or in 44.2 per cent. Hæmatemesis and intestinal hæmorrhage may be due to venous oozing or to definite ulceration from necrosis of the mucosa induced by thrombosis of the gastric or mesenteric veins. When the mesenteric veins are thrombosed, hæmorrhagic infarction may occur and give rise to paralysis of the bowel with hæmorrhagic effusion into its lumen. Gastro-intestinal hæmorrhage may be the initial symptom; this was so in 7 out of 20 cases of acute onset collected by Langdon Brown. Hæmatemesis and melæna may be frequently repeated and rapidly prove fatal. On the other hand, in cases that survive for a number of years hæmorrhages may recur from time to time during the course of the disease in spite of a very considerable collateral circulation.

Diarrhœa.—Frerichs found that diarrhœa was present in 25 out of 28 cases, while in Langdon Brown's 41 cases diarrhœa only occurred in 11. The motions are watery and may be mixed with blood. Diarrhœa is probably due to increased venous pressure and concomitant failure of nutrition in the mucous membrane of the bowel. There may be a somewhat sudden onset of acute intestinal symptoms, due to hæmorrhagic infarction and paralysis of part of the small intestine. Portal thrombosis may thus, like acute pancreatitis, simulate acute intestinal obstruction due to some mechanical cause.

In a case of Pearce Gould's,* where the superior mesenteric vein was thrombosed and the superior mesenteric artery much narrowed, there was a palpable abdominal tumor shortly before death, which was formed by the adherent coils of the lower part of the ileum extensively infiltrated with blood.

As a rule, in thrombosis of the mesenteric veins the onset of symptoms of intestinal obstruction is gradual, while in thrombosis of the corresponding artery the symptoms come on acutely. (Makins.†)

Dilatation of the Superficial Abdominal Veins.—Enlargement of the subcutaneous veins around the umbilicus, like that in ordinary cirrhosis, is noted in less than one-third of the cases of portal thrombosis. It has been thought that its rapid development is an indication of portal thrombosis, but no weight can be laid on this, or indeed on the presence or absence of dilated veins around the umbilicus.

Jaundice may be due to the same cause that gives rise to portal thrombosis, but does not depend on it and usually does not occur in uncomplicated cases.

In 41 cases it was present in 13 (Langdon Brown). It may be due to malignant disease, *i. e.*, carcinoma of the head of the pancreas, compressing or obstructing both the portal vein and the bile-duct. In only one of Langdon Brown's cases was it thought that the thrombosed vein pressed on the common bile-duct.

The urine is diminished in amount. This may be explained as due to the lowered blood-pressure, since experimental ligature of the portal vein is followed by a great fall in arterial tension. There are other factors, such as loss of blood, diarrhœa, and diminished absorption of fluid, that would also tend to produce a scanty excretion of urine. The urine is high coloured and lithatic. Alimentary glycosuria has been thought to be constantly present, and its absence to be good evidence that a suspected case is not one of portal thrombosis. Sugar, if absorbed from the intestinal tract, must pass by collateral channels straight into the general circulation; since it manifestly cannot reach the liver by means of the portal vein. The absorption from the intestines is greatly obstructed and it is very doubtful whether this test is of much value. (For consideration of this point see p. 230.)

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* Gould, A. P.: Lancet, 1902, vol. i, p. 121.

† Makins, G. H.: Brit. Med. Journ., 1898, vol. i, p. 1137.

It was certainly absent one day before death in a patient, under the care of my colleague, Dr. Penrose, with simple portal thrombosis, probably secondary to thrombosis of the hepatic veins; I have never observed it.

In a case of cirrhosis with thrombosis of the portal vein Boinet * observed paralysis of the legs; he also produced paralysis of the hind limbs in animals by aseptic ligature of the portal vein.

In some cases the symptoms are those of toxæmia resembling uræmia, and probably due to hepatic insufficiency. The symptoms are therefore the same as in the terminal stage of portal cirrhosis.

I have seen widespread cutaneous and visceral hæmorrhages in portal thrombosis.

In experimental ligature of the portal vein toxic symptoms, such as paraplegia, low temperature, and drowsiness, develop; there is also a marked fall of arterial blood-pressure which may be associated with the great engorgement of the portal system. Castaigne and Bender † refer death in experimental ligature of the portal vein to this factor and not to toxæmia.

DIAGNOSIS.

This is very difficult, and it is only seldom that a correct opinion is arrived at during life. The sudden onset of ascites or of hæmatemesis and their recurrence, accompanied by considerable splenic enlargement, might suggest it. But since these symptoms are much the same as those of cirrhosis, with which portal thrombosis is so often associated, it is difficult to differentiate between portal thrombosis and cirrhosis. Cirrhosis is so common, while portal thrombosis is so comparatively rare, that in any given case the probabilities are rather in favour of the former, even though the onset of symptoms is sudden and severe.

The sudden onset of ascites in a case of cirrhosis led me on one occasion to diagnose pylethrombosis, but the cause was tuberculous peritonitis.

In some cases of gastric ulcer profuse gastro-intestinal hæmorrhage with collapse may suggest portal thrombosis. Difficulty is likely to occur only when the gastric ulcer is acute and occurs in an adult male or in a woman who has never had any signs of gastric ulcer and is considerably past the age at which it is commonly seen.

Very profuse hæmatemesis and melæna in a soldier, aged thirty-five years, coming on suddenly at Pretoria and accompanied by a low temperature, led me to an erro-

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* Boinet: Quoted by Gorget, Rev. de Méd., 1897, p. 539.

† Castaigne and Bender: Archiv de Méd. Experim., Nov., 1899.

neous diagnosis of portal thrombosis; at the autopsy there was acute "diphtheritic" dysentery with an ulcer of similar nature in the stomach.*

In splenic anæmia the spleen is very considerably enlarged, there is anæmia of the chlorotic type, with a diminished number of leucocytes, while recurrent gastro-intestinal hæmorrhages may occur. The disease is essentially chronic while thrombosis of the portal vein is usually rapid. But in some instances of portal thrombosis, especially when the splenic vein is occluded, the spleen is greatly enlarged and there may be periodic gastro-intestinal hæmorrhages for many years, with fairly good health in the intervals.

Thus, Langdon Brown † reported the case of a woman who had had hæmatemesis at intervals of ten months for twenty years, and in whom the portal and splenic veins were found occluded.

Such cases are, however, most exceptional.

PROGNOSIS.

The diagnosis being so beset with difficulties the practical application of prognosis is very limited, but there is no doubt that the prognosis is infinitely better than in pylephlebitis. It is probable that if the process of portal thrombosis is gradual, so that a compensatory circulation can to some extent be developed before the obstruction becomes absolute, the patient has a much better chance of surviving.

If recovery from the acute symptoms occurs, the patient may live many years, even though the main trunk of the portal vein is obstructed. Thus, Langdon Brown, Osler,‡ Rogers,§ and others have recorded cases where life was prolonged for many years. In these cases the development of a collateral circulation to some extent compensates for the portal obstruction. There is, however, usually only a partial return to health, as from time to time hæmatemesis recurs and relieves the engorgement, while a very profuse gastro-intestinal hæmorrhage or a succession of hæmorrhages may prove fatal. It is also possible that the process of thrombosis may recur in the vessels forming the compensatory circulation.

TREATMENT.

Hæmatemesis and ascites should be treated on the ordinary lines as in cirrhosis. When portal thrombosis is suspected, the coagulation time and the amount of calcium salts of the blood should be determined by A. E. Wright's‖ method, and if the coagulability of the blood and the amount of calcium salts are both found to be increased, citric acid in 30-grain doses should be given three times a day in order to prevent the process of thrombosis extending. The rationale of giving citric acid is to "decalcify" the blood and so reduce its coagulability. It is important that the blood should be tested before giving citric acid, since in some cases of cirrhosis, which is the morbid lesion most frequently associated with portal thrombosis, the alkalinity and coagulating power of the blood are diminished, and no good, and possibly harm, would result from citric acid. When there is a history of syphilis, iodides and mercury may be given on the chance that there may be a gumma pressing on the portal vein or syphilitic change attacking the walls of the vein.

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* The Imperial Yeomanry Hospitals in South Africa, vol. iii, p. 193. Medical and Surgical Reports.

† Langdon Brown: St. Bartholomew's Hospital Reports, vol. xxxvii, p. 155

‡ Osler, W.: Journ. Anat. and Phys., vol. xvi, p. 208.

§ Rogers, B. M. H.: Bristol Medico-chirurg. Journ., June, 1899.

‖ Wright, A. E., and Knapp, H. H.: Lancet, 1902, vol. ii; Medico-chirurg. Trans., vol. lxxxvi, p. 1.

The operation of promoting vascular adhesions around the liver would theoretically be an ideal form of treatment for portal thrombosis, but there would probably be practical difficulties in performing it. Hæmorrhage would be likely to occur from the engorged vessels, and there is the further danger that an extension of the thrombotic process might be induced by the necessary manipulation of the peritoneum. This operation was performed in one case, but without benefit. (Langdon Brown.)

SUPPURATIVE PYLEPHLEBITIS.

Synonyms: Portal Pyæmia, Porto-pyæmic Liver Abscess (Davidson).

Suppurative inflammation may involve the portal vein together with some of its tributaries and the terminal branches in the liver; thus, in appendicitis there may be continuous suppurative pylephlebitis involving the superior mesenteric vein and the trunk and the intra-hepatic branches of the portal vein. Usually it is less extensive and may be limited to the extra-hepatic or to the intra-hepatic branches. When the branches inside the liver are alone affected, the resulting condition is practically the same as multiple abscesses due to infective embolism of the branches of the portal vein. The only difference between the two is one of degree, viz., more continuous purulent inflammation of the intra-hepatic branches of the portal vein in intra-hepatic pylephlebitis, while in multiple abscess the branches of the portal vein may be healthy for most of their extent. Since the clinical features of multiple hepatic abscesses due to intestinal infection are much the same as those of pylephlebitis, the description of the latter will suffice for a detailed account of multiple hepatic abscesses. Suppurative pylephlebitis is not a common disease; it is much less often seen than multiple liver abscesses due to infective emboli conveyed by the portal vein.

The infrequency of pylephlebitis is shown by the following statistics. In twenty years only 11 cases were met with at Guy's Hospital (Bryant *); and in thirty-three years only 12 were found at St. Bartholomew's Hospital out of 9494 postmortem examinations, or in 0.12 per cent. (Langdon Brown †).

CAUSATION.

Suppurative infection of the portal vein is generally secondary to gastro-intestinal lesions, such as ulceration and suppuration.

Thus, in 64 cases of pylephlebitis tabulated by Langdon Brown, 45, or 70.3 per cent., were associated with gastro-intestinal lesions; of the remaining 19, no cause at all was forthcoming in 7; 4 were due to gall-stones; 2 were associated with empyema; and 6 with other forms of intra-abdominal suppuration.

As might naturally be expected from analogy, infection of the portal vein is most readily produced by a collection of pus confined under considerable tension. Thus, a localized abscess in connexion with appendicitis is a relatively frequent cause of suppurative pylephlebitis, while diffuse inflammation of the peritoneum, though it may be a result, is not by itself a causal factor. In some cases pylephlebitis may be secondary to suppuration in the substance of the liver, for example, in single or

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* Bryant, J. H.: Guy's Hospital Reports, vol. liv.

† Langdon Brown, W. L.: St. Bartholomew's Hospital Reports, vol. xxxvii, p. 95.

"tropical" abscess. Suppuration in the gall-bladder and bile-ducts may also cause infective pylephlebitis. A septic wound of the main trunk of the portal vein is hardly likely to cause pylephlebitis, as rapid death from hæmorrhage would probably follow. But an exploring syringe might infect some of the intra-hepatic branches of the portal vein and so set up pylephlebitis. In a few carefully examined cases no inlet for the infection is found in the area of the portal vein.

In a case of suppurative pylephlebitis in which the primary disease was an empyema rupturing into the lung, Bryant could find no lesion of the alimentary canal, but he considered the possible explanation either that pyogenetic cocci in swallowed pus were absorbed from the stomach and thus reached the portal vein, or that exploratory punctures had passed through the empyema into the liver and thus directly infected it.

Possibly in some of the cases where no definite source of inlet is found in the intestinal tract the cause may have been pyorrhœa alveolaris and the associated swallowing of pus and micro-organisms. The pyogenetic micro-organisms could pass through microscopic lesions in the stomach into the portal vein.

Appendicitis is the most frequent cause of suppurative pylephlebitis and multiple liver abscesses. This association has been emphasized by the term "appendicular liver" (Dieulafoy *). In 64 cases of suppurative pylephlebitis collected by Langdon Brown, the appendix was the source of infection in 27, or 42.2 per cent. But appendicitis is luckily not often followed by suppurative pylephlebitis.

In 257 cases of perforative appendicitis Fitz † found suppurative pylephlebitis in 11 cases, and in 1189 cases of appendicitis operated upon in the Mount Sinai Hospital, New York, there were only 9 cases (Gerster ‡), or 0.75 per cent., which is a little higher than Treves' § estimate of 0.5 per cent.

Infection of the portal vein is more likely to occur when an abscess has formed around the appendix and the pus is under pressure. Sometimes, however, the morbid process in the appendix has begun to subside when the body of a patient with pylephlebitis is examined. Pylephlebitis may occur after the appendix has been removed, infection of the mesenteric veins having already taken place.

In a boy under the care of my colleague, Mr. Pendlebury, in St. George's Hospital, the appendix was removed on May 16 and the temperature remained normal until June 13, 1904, when it rose and a rigor occurred. The temperature continued raised until death, on July 8. There was extensive suppurative pylephlebitis.

Impaction of a pin in the vermiform appendix is a rare accident, but it appears that when it does occur there is a great likelihood of intra-hepatic suppuration; in 8 out of Mitchell's ‖ 33 cases of impacted pins in the appendix there was some form of intra-hepatic suppuration, in most instances multiple or pylephlebitic abscesses.

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* Dieulafoy: Clinique Médicale d'Hôtel Dieu, 1898. Manuel de Pathologie Interne, t. ii, p. 785, 1901.

† Fitz: Trans. Assoc. American Physicians, 1886.

‡ Gerster: Medical Record (N. Y.), June 27, 1903, p. 1005.

§ Treves, F.: Allbutt's System, vol. iii, p. 927.

‖ Mitchell: Johns Hopkins Hospital Bull., 1899, p. 35.

Gastric ulcer is very rarely the starting-point of suppurative pylephlebitis. Cases have been recorded by Carrington,[*] Bristowe,[†] Hart,[‡] West,[§] and others, and, in all, there are under ten on record.

Hart's case was specially interesting inasmuch as it was complicated by a left pyopneumothorax. In several of the other cases pylephlebitis was associated with, and probably the result of, localized suppuration set up by the gastric ulcer. In Carrington's case a gastric ulcer had eroded the substance of the liver and set up local suppuration.

Gastric Carcinoma.—Suppurative pylephlebitis very seldom follows cancer of the stomach. It may in rare instances be due to infection from a sloughing mass of carcinoma in the stomach, but this is even rarer than in simple ulcer. Legg[‖] has reported a case in carcinoma of the pylorus.

Duodenal ulcer is a most exceptional cause of suppurative pylephlebitis; Warfwinge[**] and Bryant[††] have reported cases.

Intestinal Ulceration.—The two common forms of ulceration of the small intestine, typhoid and tuberculous, very seldom set up pylephlebitis. Possibly this is in some degree accounted for by the open condition of the ulcers, which allow free drainage and discharge into the bowel. When the inflammatory process is more circumscribed in the walls of the bowel, as in amœbic dysentery, the radicles of the portal vein are in greater danger of infection.

Keen,[‡‡] in his exhaustive treatise on the surgical complications of typhoid fever, only refers to five cases of pylephlebitis. Osler[§§] has seen only one case.

It is even rarer then than solitary hepatic abscess after typhoid fever.

Dysentery very seldom gives rise to suppurative inflammation of the trunk of the portal vein. Bryant records one case. Infective emboli, however, may give rise to multiple hepatic abscess both in amœbic and in bacillary dysentery.

Penetration of the Mesenteric Veins by Infecting Foreign Bodies.—This is extremely rare; though a closely allied condition, pins perforating the vermiform appendix, is a less infrequent antecedent of suppurative pylephlebitis.

Lambron[‖‖] published a case where a fish-bone passed from the stomach into the superior mesenteric vein and set up pylephlebitis.

S. Phillips[***] has described suppuration in the spleen and pylephlebitis due to bristles in the inferior mesenteric vein.

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[*] Carrington: Guy's Hospital Reports, vol. xli.

[†] Bristowe, J. S.: Trans. Path. Soc., vol. ix, p. 279.

[‡] Hart, S.: Med. and Surg. Reports, Presbyterian Hosp., 1900, p. 150.

[§] West, S.: Trans. Path. Soc., vol. xli, p. 146, 1890.

[‖] Legg, W.: St. Bartholomew's Hosp. Reports, vol. x, p. 239.

[**] Warfwinge: (Quoted by Bernard: Gaz. d. Hôp., Aug. 14, 1897.) Schmidt's Jahrb., 1882, Bd. cxcv, S. 130.

[††] Bryant: Guy's Hosp. Reports, vol. liv.

[‡‡] Keen, W. W.: Surgical Complications and Sequels of Typhoid Fever, 1898, p. 247.

[§§] Osler, W.: Studies in Typhoid Fever. Johns Hopkins Hospital Reports, No. 3, p. 381.

[‖‖] Lambron: Archiv. gen. de Méd., 1842, p. 129.

[***] Phillips, S: Trans. Clin. Soc., vol. xxviii, p. 222.

The following **pelvic conditions** occasionally give rise to suppurative pylephlebitis: Operations on the rectum for piles, fissure, and stricture; carcinomatous and other forms of rectal ulceration; suppuration in connexion with the female genital organs, such as suppurating ovarian cysts, pyosalpinx. (De Silva,[*] Bryant.)

Suppuration of the umbilical vein in the newly born may extend into the liver and give rise to pylephlebitis. Cantlie [†] states that this condition is extremely common in Hongkong.

Suppurative and gangrenous pancreatitis may be associated with suppurative pylephlebitis. Etienne [‡] has insisted on the spread of inflammation from the pancreas to the portal vein and the production of suppurative pylephlebitis.

A man aged forty was in St. George's Hospital under the care of my colleague, Mr. Turner, in 1899, with whom I often saw the patient. On admission there was a fluctuating abscess in the epigastrium which was at once opened, and found not to be connected with the liver, but to come from the region of the pancreas. The patient improved for a time, but fever and rigors occurred; empyema on the left side and slight jaundice followed. At the autopsy the pancreas was gangrenous, there pylephlebitis and pus were found in the intrahepatic branches of the portal vein.

It may, however, be very difficult to decide whether the suppuration in the pancreas is the cause or the result of pylephlebitis. When there is some other available cause for pylephlebitis, such as appendicitis, suppuration in the pancreas must be regarded as secondary; but when suppurative pancreatitis and pylephlebitis are the only lesions present, it is often difficult to determine which occurred first.

Suppurating Mesenteric Glands and Suppuration between the Layers of the Mesentery.—Frerichs [§] describes cases, but it is open to discussion whether the glandular affection may not, at least in some instances, be secondary to the suppurative pylephlebitis. In other cases the suppuration in the portal vein and in the mesenteric glands may be both concomitant results of some intestinal or appendicular ulcer that has been overlooked or has healed.

Abscess of the Spleen.—Cases have been recorded by Frerichs,[‖] Law,[**] and Langdon Brown. It is probable that in some instances the splenic abscess is in reality secondary to pylephlebitis and not the primary cause. It seems more probable that perisplenic or subdiaphragmatic abscess on the left side may be a primary source of infection for pylephlebitis, as the pus is then under some pressure. It is possible that infective endocarditis by septic embolism of the branches of the splenic artery may lead to sloughing infarcts of the organ, and so to suppurative thrombosis of the splenic vein and pylephlebitis.

Suppuration in the Liver.—As a result of infection spreading from a large solitary abscess or from a suppurating hydatid cyst secondary

[*] De Silva: Ceylon Med. Journ., July, 1890.

[†] Cantlie, J.: Encyclopædia Medica, vol. vii, p. 41.

[‡] Etienne: Archiv. de Méd. expériment. et d'anat. path., March, 1898.

[§] Frerichs: Diseases of Liver. New Sydenham Soc., vol. ii, p. 421.

[‖] Frerichs: Diseases of Liver, New Sydenham Soc., vol. ii, p. 418.

[**] Law: Dublin Quarterly Journal, 1851, p. 238.

pylephlebitis may be set up. A suppurating hydatid is, however, much more often the cause of suppurative inflammation of the bile-ducts than of the portal vein, but may give rise to both. Suppurative cholangitis is frequently complicated by an extension of the inflammatory process to the intra-hepatic branches of the portal vein, and it is highly probable that the infection may spread by the lymphatics. In most cases where suppurative pylephlebitis complicates suppurative cholangitis it is evidently secondary and not nearly so widespread. But this tendency to pylephlebitis in suppurative cholangitis makes the latter disease even more formidable.

Gall-stones.—The usual mechanism by which cholelithiasis sets up multiple liver abscesses is by suppurative cholangitis; the multiple abscesses are then in connexion with the bile-ducts. Gall-stones in the ducts may, however, induce pylephlebitis, either by direct spread of inflammation from the ducts to the walls of the veins or through the lymphatic- or blood-vessels. In rare cases a fistulous passage between a suppurating bile-duct and the portal vein, or one of its branches, may be the method by which gall-stones in the ducts may set up pylephlebitis; in exceptional instances the gall-stone may pass into the portal vein. It is often stated that three calculi were found in the portal vein of Ignatius Loyola, but this historically interesting case has been disputed by Thudichum and Galliard.*

The lymphatics may become inflamed in cases of cholangitis, and in this way suppuration may extend along the portal spaces. The suppuration may then extend to the portal vein, and the pylephlebitis may supervene on cholangitis. This sequence of events probably occurred in a man aged forty-four whose case was described by Strangeways Pigg and myself.† In this case there was no evidence of gall-stones; but if it occurs in non-calculous cholangitis, it may presumably also occur in the calculous form. The infection may pass from the ducts by the small veins of the bile-ducts, which open into the branches of the portal vein. Bright ‡ recorded a case of calculous cholangitis in which pylephlebitis was probably produced in this way. An abscess due to cholecystitis may erode the portal vein, discharge into it, and set up pylephlebitis and multiple suppurating foci in the liver (Bristowe §).

In some instances it is very difficult to make out how cholelithiasis gives rise to suppurative pylephlebitis. A calculus may give rise to cholangitis and infection may spread to the portal vein and so set up pylephlebitis, but the calculus in the meanwhile may be passed and the cholangitis may disappear.

The following case illustrates the difficulties that may arise: A man aged fifty-one was admitted to St. George's Hospital with a history of recent gall-stone colic; he was apparently going on fairly well until he was suddenly seized with abdominal pain and collapse. I saw him when *in extremis* and thought that probably perforation of an abdominal viscus had taken place. At the autopsy there was no perforation of the viscera or peritonitis, but there was suppurative pylephlebitis without any definite cause. The larger bile-ducts were carefully examined and no ulceration or calculi were found in them; the gall-bladder contained two calculi.

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* Galliard: Médecine Moderne, Nov. 20, 1895.

† Rolleston and Strangeways Pigg: Journ. Path. and Bacteriol., vol. v, p. 221, 1898.

‡ Bright, R.: Guy's Hosp. Reports, vol. i, p. 632, 1836.

§ Bristowe, J. S.: Trans. Path. Soc., vol. ix, p. 285.

ETIOLOGY.

Sex.—The condition is commoner in males than in females, probably in accordance with the greater frequency of appendicitis in the male sex. In 72 cases, 51 were males and 21 females.

Age.—The disease usually occurs earlier in life than portal thrombosis; this may be correlated with the fact that it is most frequently secondary to appendicitis. When it occurs later in life it may be due to gall-stones or to malignant or other forms of ulceration of the colon.

In 56 cases the average age was 31.6 years; of these, 39 were males, with an average age of thirty-one years, and 17 females, with an average age of thirty-two years. Langdon Brown found that half the cases occur between the ages of twenty and twenty-nine.

MORBID ANATOMY.

The portal vein or its branches contain pus and broken-down blood-clot; sometimes there is merely pus, in other instances there is much blood-clot and but little pus, the infection and softening of the thrombus being only in an early stage. The vein walls are swollen, acutely inflamed, and from the resulting softening the vessels dilate, there is endo-, meso-, and periphlebitis; the walls may thus melt away in the suppurative process. As a result of the inflammation of the wall of the vein, blood-clot forms and becomes adherent to the intima. The clot softens down and a mixture of pus, clot, and blood results. This sanious pus may be of a reddish tint, but from changes in the hæmoglobin to something like hæmatin, the pus frequently has a dirty brown color. The suppuration may extend through the walls of the vein and lead to an abscess outside the vein; thus in some cases of pylephlebitis there is an abscess behind the pancreas; this, though sometimes described as a cause, is usually a result, of pylephlebitis.

As a very rare accident in pylephlebitis Hodenpyl's * case may be referred to. A young man aged twenty-five died from rupture of the portal vein, the abdominal cavity being filled with pus. The pylephlebitis was due to streptococcal infection.

The extent of the vein affected may vary very greatly; a localized part of the portal vein or one of its branches may be found full of pus and shut off from the remainder of the vein by a partition of firm clot. Thus, when the trunk of the portal vein is suppurating the splenic vein is sometimes cut off from the infective process by a firm clot at its junction with the portal vein. Occasionally there may be two foci of suppuration, one near the periphery, the other in the intra-hepatic branches of the portal vein, while the intervening parts of the vein are healthy In such cases the intra-hepatic focus is due to emboli derived from the other focus of suppuration.

The liver is nearly always involved, either by an extension to it of the suppurative inflammation of the portal vein, or by secondary abscesses due to emboli from the portal vein. In very rare cases, of which I have examined one, the liver may show no signs of acute inflammation; this, however, was a case where suppurative inflammation had only recently supervened on thrombosis of the vein.

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* Hodenpyl: Medical Record (N. Y.), July 23, 1898.

The liver is nearly always enlarged and may be double its natural weight. There is usually perihepatitis due to extension of inflammation to the capsule, which commonly leads to adhesions to the diaphragm. The surface of the organ is usually smooth, but abscesses may project somewhat from the surface and, if seen during the course of an operation, may suggest multiple new-growth. Over these abscesses there may be a thin layer of recent and adherent lymph. The liver has a mottled appearance; the abscesses, or the areas where suppuration is about to take place, are of a palish-yellow colour. Before abscess formation occurs coagulation necrosis of the liver cells may render parts of the liver firm and like nodules of secondary carcinoma. On section multitudes of small abscesses, varying in size from a millet-seed to a walnut, may be seen, due to the suppurating portal canals being cut transversely. If the course of the portal canals be followed, suppuration is seen to spread out from the portal fissure into the liver like the branches of a tree. There is often dark-green staining of the portal canals from decomposition. One lobe or only a limited part of a lobe, or again the whole liver, may show abscesses. The left lobe escapes more often than the right. From the coalescence of a number of originally separate abscesses a large (areolar) abscess may be formed. In other instances the abscesses are so close to each other that a honeycombed condition of part of a lobe results.

The abscesses due to pylephlebitis may resemble at first sight some cases of suppurative cholangitis with abscesses in the liver. A careful examination of the bile-ducts and portal vein and their branches inside the liver should therefore always be made in any case of doubt. Similarly any difficulty in differentiating between tuberculous abscesses in connexion with the bile-ducts and pylephlebitis can, if necessary, be settled by microscopic examination. Multiple pyæmic abscesses, due to emboli conveyed by the hepatic artery, are small and hardly ever resemble pylephlebitis. The condition of multiple abscesses, due to embolism of the portal vein from some foci in its tributaries, only differs from pylephlebitis in the absence of extensive phlebitis of the portal vein; in other respects the two conditions are practically identical.

Leakage or rupture of the small abscesses on the surface of the liver will set up peritonitis, either general or local, such as a subphrenic abscess. When the diaphragm is previously adherent to the liver extension of infection may set up pleurisy, empyema, or suppuration in the lower lobe of the lung, usually, of course, on the right side. Abscesses on the under surface of the liver may give rise to perihepatic or subhepatic collections of pus.

Histology.—Microscopically the portal vein is filled with fibrin and leucocytes, its walls are infiltrated with small round cells, and may be destroyed. In the liver the portal space is similarly affected and small cell infiltration extends between the lobules and around the intralobular branches of the vein. The liver cells at the periphery of the lobules are compressed and become elongated and look somewhat like oval connective-tissue cells; the small cell infiltration spreads between the liver cells, which undergo degenerative changes. Micro-organisms are seen in the vessels and between the cells.

Bacteriology.—Streptococci, staphylococci, diplococci, and Bacillus coli communis in pure cultures have been met with. In dysenteric cases the Amœba coli and other micro-organisms, and in cases after typhoid fever the Bacillus typhosus, have been found. Mixed infections are not uncommon.

In Norris'* case two anaërobic micro-organisms, a streptococcus resembling the Micrococcus fœtidus and a new bacillus, were regarded as the cause of suppuration.

The Spleen.—There is usually some enlargement, which may be explained as due to the general septic or toxic condition. In cases where the splenic vein is occupied by suppurating clot or where the junction of that vein with the trunk of the portal vein is excluded the spleen may be very large from venous obstruction. Abscesses are sometimes found in the spleen, and may either be part of suppurative pylephlebitis or its starting-point.

Peritonitis is common; according to Bryant, it occurs in 50 per cent. of the cases. It may be due to rupture of the pylephlebitic abscesses on the surface of the liver and may be general or localized. Peritonitis is also frequent around the primary lesion, such as appendicitis, pyosalpinx, etc.

The pancreas is usually healthy; it has occasionally been found to contain abscesses, probably as a result of suppurative phlebitis of the splenic vein spreading into its pancreatic tributaries. An abscess behind the pancreas and around the portal vein is sometimes seen as a result of suppurative pylephlebitis. In some instances an abscess due to suppurative pancreatitis may be the cause of suppurative inflammation of the portal vein.

Pleura.—The right pleura is seldom healthy; there may be recent pleurisy, with or without a serous or purulent effusion. Inflammation readily spreads through the diaphragm from the liver. Rupture of a pyæmic abscess in the lung may set up an empyema or even a pyopneumothorax.

Lungs.—The right lung may show collapse and hypostatic congestion of the base; abscesses with surrounding pneumonic consolidation may be due to direct extension through the diaphragm, or in rare instances to general pyæmia, some pylephlebitic abscesses having discharged into the hepatic veins.

Pylephlebitis with multiple small abscesses in the liver may give rise to general hæmic infection and secondary abscesses in other organs. According to Langdon Brown, this occurs in 40 per cent. of the cases. Reference may be made to two cases of secondary cerebral suppuration.

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* Norris: Journ. of Medical Research, July, 1901.

Thus, in an undoubted case, recorded by Norman Moore,* of pylephlebitis due to appendicitis, there were numerous small abscesses in the brain; and in Cassirer's † case the symptoms were those of a cerebral lesion, the cause—a fish-bone in the appendix—being only found at the autopsy.

CLINICAL PICTURE.

The onset of symptoms is more often sudden than gradual. In 43 cases analyzed by Langdon Brown the onset was acute in 27, gradual in 15. It may be ushered in by rigors, but usually abdominal pain is the earliest symptom. The initial symptoms may be those of the disease—most often appendicitis—causing the pylephlebitis. Thus, pain, vomiting, and abdominal distension may be the first indications that anything is amiss. In a typical case there should be, first, evidence of the primary cause, such as appendicitis; secondly, the development of a pyæmic state; and, thirdly, evidence that the liver is involved. (Taylor.‡)

Course.—After the onset the patient passes into a "septic" state resembling pyæmia; rigors may be present at first, but usually disappear later. After a time most cases show signs of hepatic disease in pain, enlargement, and tenderness; the septic condition continues, and signs suggesting empyema, pneumonia of the right lung, or peritonitis may develop. Gradually increasing weakness often passing into coma precedes death.

Duration.—There is considerable variation in the duration of the disease. The average of the cases collected by Langdon Brown § was forty-seven days, the shortest being three days. In an exceptional case of Goodhart's,‖ where partial recovery was taking place, the disease lasted two hundred and ninety-six days.

Signs.—The patient has an abdominal facies, looks sallow, ill, and anxious, and has a raised temperature. The type of fever varies very widely; it may be continuous, intermittent, or remittent. Towards the close it may be subnormal; it is interesting in this connexion to remember Hanot's view that in infections with the colon bacillus the temperature is depressed. The pulse is soft, compressible, and rapid (100 to 140). The respirations are quickened. When the disease has lasted some time there will be wasting and great prostration.

Rigors are seen in a majority of the cases.

In 42 cases Brown found them in 29, or 69 per cent.; in Bryant's series they were present in half the cases.

The rigors occur during the earlier part of the illness and tend to disappear in the later stages. They are followed, as in tropical abscesses and in malaria, by profuse sweating, but are uncontrolled by quinine.

Jaundice occurs in less than half the cases and is often quite slight, transient, or only noted late in the course of the disease, and can be explained as due to the general toxæmia. In some cases it is marked and may be due to cholangitis, concomitant obstruction of the bile-duct by calculi, or to pressure of an abscess on the common bile-duct.

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* Norman Moore: Trans. Path. Soc., vol. xxxiii, p. 186.

† Cassirer: Medical Press, Oct. 30, 1901.

‡ Taylor, F.: Guy's Hospital Reports, vol. lvi, p. 109.

§ Langdon Brown: St. Bartholomew's Hospital Reports, vol. xxxvii.

‖ Goodhart: Trans. Path. Soc., vol. xxxii, p. 137.

In 44 cases, tabulated by Langdon Brown, there was jaundice in 19; in four of these it was very slight or transient, while in five it was an initial sign.

Clinically the *liver* can be felt to be enlarged in more than half the cases; Frerichs says in 75 per cent., Bryant in 60 per cent., and Langdon Brown, who collected a larger number of cases, in 57 per cent., of the cases. The enlargement is usually uniform, but in a few instances elevations, due to projecting abscesses, are distinctly palpable. The enlarged liver may reach down to the umbilicus and may lead to upward displacement of the diaphragm, and thus to collapse of the lower lobe of the right lung and even to displacement of the apex of the heart. A friction rub from inflammation of its peritoneal surface may be heard over the liver. Pain and tenderness in the hepatic region are generally met with, but they may be absent. Local tenderness, which is sometimes present when the liver cannot be felt to be enlarged, is more valuable as evidence of hepatic suppuration than pain referred to the right hypochondrium.

Enlargement of the spleen is sometimes observed; in 33 cases it was noted in 9 (Langdon Brown). When there is very considerable enlargement, hæmatemesis should be expected; as the size of the spleen may be due to obstruction of the splenic vein, which would also lead to engorgement of the cardiac end of the stomach by interfering with the return of blood through the vasa brevia veins.

Vomiting is often met with early in the course of the disease. It was present in 24 out of 42 cases collected by Langdon Brown, being an initial symptom in 11. It is not so much a sign of pylephlebitis as of the disease, such as appendicitis, responsible for suppurative inflammation of the portal vein.

In rare instances a *gastric ulcer* may be secondary to pylephlebitis and even go on to perforation.

In a man aged fifty-four examined by me in 1897, with suppurative pylephlebitis secondary to appendicitis, there was perforative peritonitis due to rupture of a gastric ulcer, which, in its turn, was evidently due to thrombosis of a gastric vein.

Diarrhœa is fairly common, occurring in about half the cases. Blood is occasionally seen in the stools. *Constipation* is rarely noticed. *Hiccough* may be a troublesome feature.

Tympanitic distension of the abdomen may occur from peritonitis and will obscure enlargement of the liver and spleen.

Ascites is rare. It is more likely to occur in cases that last a considerable time, and where suppuration supervenes on thrombosis of the portal vein. Although clinically ascites is seldom seen, there may be a small amount of ascitic effusion, due to local acute peritonitis over the abscesses in the liver.

Thoracic Signs.—There may be an audible friction rub over the right side of the chest from extension of inflammation through the diaphragm to the pleura. The pressure exerted by the enlarged liver may lead to bulging of the chest wall and to collapse of the lung, imitating pleurisy with effusion. In some cases there may actually be a purulent effusion into the pleura or the lung may contain abscesses. It is not to be wondered at that such cases may be diagnosed as empyema or septic pneumonia.

Blood.—There is some degree of secondary anæmia, especially in prolonged cases. In the reported cases leucocytosis is not mentioned as a rule, but it would naturally be expected. It was present in 3 out of 4 cases referred to by Langdon Brown; and in 4 cases, associated with appendicitis, French * found marked leucocytosis (24,000) in one and in the others counts of 18,000, 12,000, and 10,500. Micro-organisms may be found in the blood when pyæmia has developed, but this only occurs near the end of the case.

Urine.—Albuminuria is sometimes found and is due to septic absorption. When there is jaundice bile-pigment will be found in the urine. Indicanuria may be present, and excessive urobilin has been observed. (Goodfellow.†)

Termination.—Towards the end the patient passes into a semicomatose condition of stupor. Death may occur from peritonitis, from coma and increasing weakness, or in rare instances suddenly from collapse after sudden hæmatemesis or melæna.

DIAGNOSIS.

A septic or pyæmic state with evidence that the liver is affected, in a patient who has had appendicitis or some other intra-abdominal condition known to cause pylephlebitis, forms the broad outline of the disease. Enlargement and tenderness of the liver, with pain, fever, and a pyæmic state, not due to any other cause, should suggest suppurative pylephlebitis. Pyæmia from bone and ear disease and infective endocarditis must be excluded. But a diagnosis is not always possible, and since hepatic enlargement is absent or is not detected in a certain proportion of cases of pylephlebitis, there may be nothing to direct attention to the liver. The difficulty of diagnosis is shown by the fact that in 20 cases examined after death at Guy's Hospital a correct diagnosis during life was only arrived at in two instances during life.‡

Differential Diagnosis.—In *tropical abscess* there is not such rapid emaciation and prostration as in pylephlebitis, fluctuation may be felt, a history of past dysentery rather than of appendicitis should be forthcoming, and the spleen is not enlarged, as it may be in pylephlebitis. In many cases it is impossible to be certain whether there is a single abscess deeply situated in the liver or pylephlebitis with multiple hepatic abscesses. As mentioned above, the history of pre-existing dysentery is generally in favour of a single abscess, but it must be remembered that dysentery may be followed by multiple abscesses in the liver like those of pylephlebitis; this was notably the case in the dysentery seen in South Africa during the Boer War of 1899–1902.

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* French, H. S.: Medico-Chir. Trans., vol. lxxxvii.

† Goodfellow: Medical Chronicle, vol. xxxvii, p. 288, 1903.

‡ Bryant, J. H.: Guy's Hospital Reports, vol. liv.

In *hepatic suppuration* secondary to appendicitis multiple foci of suppuration are the rule, but in exceptional instances a large areolar abscess, probably due to the union of originally independent abscesses, results. In a given case with hepatic enlargement, fever, rigors, and pain, the question whether the condition is one of multiple abscesses, pylephlebitis, or a single abscess is a very difficult one to decide, and probably the patient should be given the benefit of the doubt and abdominal exploration be undertaken. Œdema of the chest wall or definite fluctuation justifies a diagnosis of a large and probably single abscess.

In *suppurative cholangitis* jaundice is commoner, appears earlier, and is more prominent than in pylephlebitis. Splenic enlargement may occur in both, but is more likely to be marked in pylephlebitis. A history of cholelithiasis and biliary colic is in favour of suppurative cholangitis.

Typhoid Fever.—In typhoid fever the agglutination (Widal's) reaction with typhoid bacilli should be present, while rigors and jaundice, though not unknown, are decidedly rare. A positive agglutination reaction may occur in pylephlebitis when the patient has had typhoid fever some time previously.

In a woman aged twenty-eight, who died of pylephlebitis under Dr. F. Taylor's * care, there was a positive agglutination reaction with typhoid bacilli although she had not had typhoid fever.

Pylephlebitis may closely resemble typhoid fever, especially when there is blood in the stools; in such cases the absence of the agglutination reaction and of Ehrlich's diazo reaction in the urine would help to eliminate typhoid fever. Bryant lays stress on the difference between the pulse, temperature, and respiration rates in pylephlebitis and in typhoid fever; the pulse rate is low (80) in enteric, high (140) in pylephlebitis.

In *infective endocarditis* murmurs are occasionally absent and the aspect of the case is one of pyæmia of obscure origin; in such cases, when accompanied by enlargement of the liver and spleen, the resemblance to pylephlebitis may be considerable. In the majority of cases of infective endocarditis, however, there is evidence of cardiac disease, and there is little difficulty in distinguishing between it and pylephlebitis.

In chronic cases of *malarial infection* the enlarged and sometimes very tender liver and the raised temperature associated with shivering and sweating may lead to considerable difficulty in diagnosis. Malaria should be recognized by the presence of the parasite in the blood and improvement under quinine, while the patient's condition is not so bad as in pylephlebitis.

Intra-thoracic conditions, such as pleural effusion, empyema, pulmonary abscess or pneumonia, may be diagnosed as the sole condition, from physical signs depending on the spread of inflammation from the liver in pylephlebitis. In the same way a subdiaphragmatic abscess may be recognized, while its underlying cause—multiple pylephlebitic abscesses—is unsuspected.

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* Taylor, F.: Guy's Hospital Reports, vol. lvi, p. 109.

Malignant disease of the liver may imitate pylephlebitis when fever and rigors accompany rapid increase of the malignant growth. A case of secondary endothelioma of the liver resembling pylephlebitis is described in the heading of the diagnosis of malignant disease of the liver.

In cases of acute *cirrhosis* the enlarged and tender liver and the presence of fever may imitate pylephlebitis. (Carrington.*)

PROGNOSIS.

Since diagnosis is difficult, more cases are recognized on the postmortem table than during life, and grave doubt must exist as to the nature of cases regarded as suppurative pylephlebitis which have recovered without any laparotomy and examination of the liver. It is in the highest degree improbable that widespread suppuration of the portal vein would be followed by recovery, and the general consensus of opinion is that the disease is uniformly fatal. Conceivably this verdict may require some modification in the light of more frequent observations of the state of the liver as seen in the course of exploratory laparotomies. In isolated cases recovery has occurred where multiple abscesses were thought to exist, but some question must arise whether suppurative inflammation of the portal vein was actually present in these instances.

Treves † opened the abdomen of a girl aged fifteen with pylephlebitis after appendicitis and observed appearances pointing to abscesses in the liver; the patient recovered. West ‡ recorded recovery after multiple abscess secondary to appendicitis had been opened. In a boy aged eighteen years who died after ten months' illness there was occlusion of the portal vein and scars with caseous centres in the liver; this case was regarded by Goodhart § as suggesting that suppurative pylephlebitis, due to appendicitis, had ended in cicatrization. Death was due to suppuration connected with ulceration and perforation of the descending colon, possibly secondary to portal obstruction, and lardaceous disease.

Possibly some cases recover that are not sufficiently well marked to be recognized, but there is no avoiding the conclusion that the prognosis can hardly be worse than in this disease.

TREATMENT.

When the disease is recognized treatment is usually confined to relieving pain and other symptoms. Langdon Brown and Gerster ‖ have employed antistreptococcic serum without any good results. Its use is perhaps worth trying on the chance that the infection of the portal vein is a pure streptococcal one, but in most cases there is a mixed infection. In the future it is probable that treatment with polyvalent sera, viz., from animals immune against various strains of micro-organisms of the same and of different species (streptococci, Bacillus coli), may be employed. Since it is difficult or impossible to be sure that symptoms of pyæmia with hepatic enlargement after appendicitis are not due to a single abscess, operative interference gives the patient a chance of recovery. Further, it is possible that success might follow the opening and draining of several abscesses, as in West's case. When operation is undertaken, the liver should be freely exposed. Aspiration through the abdominal wall is not only fallacious, but may be dangerous.

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* Carrington: Guy's Hospital Reports, Series iii, vol. xxvii, 1884.

† Treves: Allbutt's System, vol. iii, p. 927. Brit. Med. Journ., 1894, vol. i.

‡ West, S.: Trans. Clinic. Soc., vol. xvii, 126.

§ Goodhart: Trans. Path. Soc., vol. xxxii, p. 137.

‖ Gerster: Medical Record (N. Y.), June 27, 1903.

Prophylactic treatment is most important, and consists in the early and radical removal of conditions, such as appendicitis, likely to induce suppurative pylephlebitis. During such operations removal of any suppurating veins in the immediate neighbourhood is an important step in preventing the spread of infection from the intestinal branches to the trunk of the portal vein. This was carried out in two cases of appendicitis which recovered (Gerster). It is also important not to disturb the parts unnecessarily, so as to avoid detaching a thrombus and producing embolism of the intra-hepatic branches of the portal vein.

OTHER AFFECTIONS OF THE PORTAL VEIN.

Embolism; Endophlebitis; Calcification; Parasites.

EMBOLISM.

Embolism of the intra-hepatic branches of the portal vein is frequent in suppurative inflammation of the intestinal tributaries of the portal vein and accounts for multiple abscesses in the liver after appendicitis, etc. In most cases the emboli are small and do not themselves attract attention. Similarly embolism plays an important part in the production of secondary growths in the liver in carcinoma of the stomach and intestine. Sometimes large embolic masses of clot may be found in the main intra-hepatic branches of the portal vein.

In 17 cases of infarcts in the liver Chiari * found that 15 were due to embolism of the portal vein, the emboli being derived from thrombosis in its peripheral tributaries, such as the hæmorrhoidal, gastric, splenic and mesenteric veins.

ENDOPHLEBITIS.

Acute inflammation of the portal vein is practically the same as pylephlebitis. *Chronic endophlebitis* of the portal vein is not uncommonly associated with hepatic cirrhosis, and may be explained as the result of increased blood-pressure in the vein, combined perhaps with degeneration and hyperplastic changes due to the action of toxic bodies. There is a certain amount of chronic endophlebitis of the portal vein in long-standing backward pressure from tricuspid regurgitation, in mitral disease, and in obstructive pulmonary diseases, such as emphysema. According to Borrmann,[*] syphilitic disease of the liver may extend into the portal vein and set up syphilitic endophlebitis of its walls. But in a certain number of cases the endophlebitis is primary and the liver merely shows a secondary atrophy. The essential cause of the chronic inflammatory change in the vein is somewhat obscure, and has been referred to a number of causes. Possibly syphilis may play a part in some cases, but of this there is no convincing proof. In general paralysis of the insane, which is regarded by Bruce [†] and Ford Robertson [‡] as a chronic toxæmia of intestinal origin, chronic endophlebitis has been described by Angiolella.[§] Inflammation may also spread into the vein walls from chronic peritonitis.

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* Chiari: Zeitschrift f. Heilkunde, Bd. xix, S. 475.

In splenic anæmia endothelial hyperplasia may spread from the blood sinuses in the spleen into the splenic and portal veins; as a result of these changes the terminal cirrhosis of the liver in splenic anæmia (Banti's disease) has been explained. Chronic endophlebitis may lead to calcification and to thrombosis; the latter result is a fact of practical importance.

CALCIFICATION.

This is a sequel of long-standing endophlebitis and is analogous to secondary calcification in endarteritis. It is probably much commoner than is usually thought. I have seen it microscopically in cases where there was not sufficient infiltration to attract attention in the postmortem room. Its occurrence has been known for a long time. Frerichs[||] gives quite a number of references to "ossification" or calcification of the portal vein. The calcareous plates or spicules may project into the lumen of the portal vein and set up thrombosis. But calcification may be very extensive without any trace of thrombosis, and it must not be assumed, as Lancereaux [**] does, that calcification of the wall of the portal vein is merely the result of thrombosis of the vein and of subsequent changes.

A marked degree of chronic endophlebitis with calcification of the splenic and portal veins occurred in a man aged fifty-three who died in St. George's Hospital after a surgical operation for hydrocele. The splenic vein was greatly dilated and the splenic artery was very calcareous and had three aneurysms on it. The spleen was much enlarged (42 ounces) and fibrotic. The liver (37 ounces) was scarred, and to the naked eye suggested syphilis, but microscopically it showed multilobular cirrhosis of old standing and no evidence of syphilis. The colon showed extensive ulceration, possibly of vascular origin, but there was no thrombosis in any of the branches of the mesenteric arteries or in any part of the portal vein or its branches.[††]

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[*] Borrmann: Deutsche Archiv f. klin. Med., 1897.

[†] Bruce, L. C.: Brit. Med. Journ., 1901, vol. i, p. 1600.

[‡] Ford Robertson: Brit. Med. Journ., 1901, vol. i, p. 1602.

[§] Angiolella: Il Manicomio Moderna, 1894, 1895. Quoted by Ford Robertson.

[||] Frerichs: Diseases of the Liver, vol. ii, p. 402. Translated by New Sydenham Soc.

[**] Lancereaux: Traité des Maladies du Foie et du Pancreas, p. 571, 1899.

[††] Trevor, R. S.: Trans. Path. Soc., vol. liv, p. 302.

PARASITES IN THE PORTAL VEIN.

Bilharzia hæmatobia, endemic in Egypt, Natal, Mauritius, and Syria, may be found in the trunk of the portal vein or in its hæmorrhoidal tributaries, while the walls may contain the ova. The liver may show slight cirrhosis,* but there are no symptoms associated with the presence of the worms or their ova in the portal vein. The liver fluke (Distomum hepaticum) was described in a case quoted by Budd † as being found in the portal vein, but it is conceivable that a dilated bile-duct was mistaken for the vein.

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[*] Symmers: Journ. Path. and Bacteriol., vol. ix, p. 237.

[†] Budd: Diseases of the Liver, 1857.

MORBID CONDITIONS OF LYMPHATIC VESSELS AND GLANDS.

MORBID CONDITIONS OF THE LYMPHATIC VESSELS.

Comparatively little is known on this subject, and primary affections of the lymphatics of the liver are not recognized. That the lymphatics must frequently suffer when the portal spaces are affected by morbid processes such as inflammation and tuberculosis is clear, and there is evidence that this is so in the enlargement of the lymphatic glands in the portal fissure.

Pericholangitis is very closely connected with, if indeed it is not practically synonymous with, lymphangitis of the portal spaces. Thus, the glands in the portal fissure are enlarged in hypertrophic biliary cirrhosis, tuberculous cavities in the liver, cholangitis, and pylephlebitis, all of which are inflammatory lesions involving the tissues and the portal canals around the bile-duct and portal vein. In a case of splenic anæmia in which the spleen showed most extensive endothelial proliferation Bovaird * figures a similar endothelial proliferation in the lymphatic vessels of the portal spaces.

New-growth may sometimes be seen working its way into the liver, against the lymph-stream, along the lymphatics of the portal fissure; more commonly the glands in the portal fissure become infected secondarily to a growth in the liver, the infecting cells travelling in the normal direction along the lymphatic vessels. Distension of the lymphatic vessels in the portal spaces is occasionally due to obstruction; it has also occurred from torsion of the bile-duct in hepatoptosis. In diabetic lipæmia I have seen the lymphatics of the portal spaces graphically mapped out by the contained fat. Maresch † has described a pedunculated lymphangioma which was removed from the right lobe of the liver of a girl aged five years.

THE LYMPHATIC GLANDS IN THE PORTAL FISSURE.

Any enlargement of these glands is of importance inasmuch as pressure may thus be exerted on the bile-ducts and jaundice set up. Thus it has been thought, but probably without sufficient reason, that the jaundice occasionally seen in the roseolous stage of syphilis may be due to swelling of the glands in the portal fissure. Enlargement of the portal glands may occur in lardaceous disease and leukæmia, but cannot be credited with producing jaundice or ascites by compression of the bile-duct or portal vein.

Enlargement of the portal lymphatic glands may be due to vari-

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* Bovaird: American Journ. of Med. Sciences, vol. cxx, p. 391.

† Maresch: Zeitschrift f. Heilkunde, Bd. xxiv, S. 39, 1903.

ous conditions, chiefly inflammatory, inside the liver, such as abscess, pylephlebitis, suppurative cholangitis, tubercle, hypertrophic biliary cirrhosis, and primary carcinoma. As already mentioned, new-growth may extend into the portal fissure along the lymphatic vessels against the flow of lymph, and occasionally infiltration of the portal lymphatic glands may be secondary to carcinoma in the peritoneal cavity, and may give rise to jaundice.

CHRONIC VENOUS ENGORGEMENT OF THE LIVER.

Synonyms: Nutmeg Liver, Cardiac Liver, Cyanotic Atrophy, Hepatic Asystole.

The term red atrophy has been applied to the small nutmeg liver seen in long-standing cases of backward pressure, but is unfortunate in that it may lead to confusion with an entirely different condition, viz., the red atrophy seen in acute (yellow) atrophy. An old and now forgotten name for the condition of the liver was hypertrophy of the white substance.[*]

Though this is not a primary morbid condition of the liver, it may be convenient to describe it in considerable detail. Chronic venous engorgement of the liver is practically always secondary to obstructive heart or lung disease, and the symptoms due to the hepatic condition are added to those of the primary disease. Hanot[†] has suggested the term hepatic asystole for those cases in which the hepatic symptoms are more prominent than those of the primary cardiac disease.

ETIOLOGY.

Cardiac Lesions.—Obstructive or regurgitant mitral disease, and some diseases of the myocardium, such as dilatation of the left ventricle due to alcoholic excess, give rise to backward pressure, tricuspid regurgitation, and chronic hepatic engorgement. When tricuspid stenosis is present, it is practically always secondary to mitral stenosis; in these cases the hepatic engorgement is extremely marked. Mitral stenosis is of all common cardiac lesions the most effective in producing chronic venous engorgement of the liver.

Lung Lesions.—Obstruction to the passage of blood through the pulmonary artery and its branches in the lungs gives rise first to hypertrophy of the right ventricle, but eventually this compensation becomes strained, the right ventricle dilates, and tricuspid incompetence results. This train of events most often follows chronic bronchitis and emphysema, the pneumokonioses, and sometimes chronic interstitial pneumonia. It is remarkable that in ordinary pulmonary tuberculosis chronic venous engorgement is not more often seen. My own experience is that it is rare to see it in cases of chronic pulmonary tuberculosis, but Gilbert and Weil,[‡] in a study of 25 livers, found that in 6 the naked-eye appearances were those of a typical nutmeg liver, and that in 5 more the microscopical appearances were undoubted. Possibly those cases where it occurs are complicated by alcoholic dilatation of the heart.

Other Factors.—It is possible that a tumor or aneurysm may press

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[*] Compare Hope: Principles and Illustrations of Morbid Anatomy, p. 102, 1834.

[†] Hanot: Bull. de la Soc. Méd. d. Hôp., 1895, p. 409.

[‡] Gilbert and Weil: Archiv de Méd. expériment. et d'Anat. path., tome xiv, p. 729, Nov., 1902.

on the small segment of the inferior vena cava between the entrance of the hepatic veins and its termination in the right auricle; but it is extremely rare for an intra-thoracic growth to obstruct the inferior cava. I have seen nodules of secondary growth on the diaphragm in close contact with the inferior cava. In thrombosis and in stricture of the orifices of the hepatic veins (*vide* p. 49) a nutmeggy condition of the liver may be produced. Obstruction of the inferior vena cava where it receives the two hepatic veins may have the same result.

But in a marked example of obliteration of the inferior vena cava recorded by Osler,* in which the orifices of the hepatic veins were very greatly narrowed, the liver was cirrhotic rather than nutmeggy.

Inside the liver the pressure of malignant growths or hydatid cysts may lead to local areas of chronic venous engorgement. It is possible that marked displacement of the heart in pleural or pericardial effusion, by producing kinking of the inferior vena cava, might lead to venous stasis in the hepatic veins of the liver as well as in the other tributaries of the inferior cava. It has been suggested that pericardial adhesions may lead to torsion of the inferior vena cava and so to chronic venous engorgement. It has been thought that any pre-existing morbid condition of the liver, such as may result from alcoholism, biliary calculi, or malaria, renders the organ more prone to suffer from the effects of backward pressure in any given case of tricuspid incompetence.

MORBID ANATOMY.

Adhesions between the upper surface of the liver and the diaphragm are frequently seen. They are the legacies of past attacks of acute perihepatitis which are not uncommonly due to the spread of inflammation through the diaphragm from acute pleurisy or pericarditis. The upper surface of the right and left lobes often shows a depression corresponding to an hypertrophied and dilated heart. The peritoneum covering this depressed area is often thickened and opaque as the result of increased and long-continued friction. In cases of universal chronic perihepatitis or "iced liver" (*vide* p. 170) there is usually chronic venous engorgement, but this condition should be kept distinct from uncomplicated nutmeg liver, in which there is no general perihepatitis.

Size.—After death the liver is sometimes larger than natural, but is smaller than in life. During life the liver is distensible and may vary in size very considerably within short periods as the result of alterations in the amount of backward pressure. After death, when rigor mortis has set in, coagulation of the protoplasm of the liver cells gives a firmness to the organ which does not represent its condition in life.

Sir Lauder Brunton† found that if artificial circulation be kept up through the portal vein of an animal just killed, the liver will enlarge and diminish in response to variations in the pressure exerted, almost as if it were a sponge, and much in the same way as it does in cases of pulsating livers.

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* Osler: Journ. Anat. and Physiol., vol. xiii, p. 291.

† T. Lauder Brunton in Murchison's Diseases of the Liver, 3d edition, 1885, p. 134.

In the later stages the liver becomes smaller; this is associated with, and most probably due to, atrophy of the liver cells and not to the contraction of the fibrous tissue in the portal spaces, as suggested by Legg.* The liver is of a darkish purple colour externally and is rather firmer than natural. Dilated veins may be seen on the surface, and no doubt their prominence is largely due to atrophy of the surrounding liver tissue. As a rule, the surface of the organ shows depressed lines of atrophy, and may thus become slightly uneven, suggesting to the naked eye early cirrhosis. The characteristic mottling is generally not well seen externally. If there has been long-standing ascites, the serous covering of the liver will be thickened or opaque.

On section the organ contains an unusual amount of blood and presents the characteristic "nutmeggy" appearance, which depends on the fact that the sublobular and intralobular veins are dilated and appear as dark purple spots or streaks according as they are cut transversely or longitudinally, while the other parts of the lobules, being stained with bile or infiltrated with fat, are paler than natural. This contrast between the deeply coloured and the pale areas resembles the section of a nutmeg. In a typical case the centre of the lobule appears as a dark spot; this is surrounded by a whitish-yellow margin due to fatty and slightly bile-stained liver cells. In other cases there is a coarse nutmeg appearance due to alternation between areas of engorgement and areas showing fatty change and bile staining. The hepatic veins are dilated and larger than natural and their walls are thicker and more opaque; this phlebosclerosis is evidently the result of chronic engorgement and is accompanied by atrophy and condensation of the hepatic tissue immediately around the vein walls.

Opponet, in a thesis† on hepatic asystole, puts forward the view that the incidence of hepatic manifestations in a case of heart disease is determined by a peculiar arrangement of the hepatic veins at their entry into the inferior vena cava; this anatomical disposition he regards as congenital and as fairly common. It seems, however, more natural to regard the size and manner of the openings of the hepatic veins into the inferior vena cava as the results of backward pressure.

In backward pressure in the inferior vena cava the main stress usually falls on the legs; occasionally, however, the renal veins are chiefly involved, as shown by persistent albuminuria without any corresponding nephritis on histological examination, while in cases of hepatic asystole the hepatic veins suffer chiefly. In backward pressure the brunt may fall on any one of these three branches of the inferior vena cava.

Occasionally a liver which is the subject of chronic venous engorgement is also distinctly cirrhotic. Thus, a patient with cirrhosis may die with alcoholic dilatation of the heart or with backward pressure from cardiac failure due to other causes. The two conditions, nutmeg and cirrhotic livers, are both common and sometimes coincide, but chronic venous engorgement alone does not cause real cirrhosis. This is my firm conviction from an examination of a large number of livers both post-mortem and microscopically.

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* Legg: Med.-Chirurg. Trans., vol. lviii, p. 352.

† Paris, 1895.

The Question of "Cardiac Cirrhosis."—The question whether chronic venous engorgement *per se* leads to cirrhosis of the liver has given rise to very considerable discussion, for a full account of which the reader should consult Piery's thesis.[*] In 1840 Becquerel[†] considered that chronic venous engorgement was the cause of half the number of cases of cirrhosis examined by him; his view was supported by Rokitansky,[‡] Henle,[§] and others. It is possible, as suggested by Wickham Legg, that at this time cirrhotic and nutmeg livers were not differentiated from each other. In 1845 Budd[‖] and in 1848 Handfield Jones definitely separated cirrhosis and chronic venous engorgement from each other and stated that chronic venous engorgement did not give rise to cirrhosis.

Considerable discussion has ranged as to the locality of increased fibrosis in cardiac cirrhosis. Rokitansky, and Sabourin[**] described it as centrilobular, while English observers—Handfield Jones,[††] Green,[‡‡] and Legg[§§]—considered that it was perilobular but not genuine multilobular cirrhosis. Numerous observations prove that chronic venous engorgement of the liver may exist for prolonged periods without producing any fibrosis at all, or only a slight fibrosis, as seen microscopically, which can be satisfactorily accounted for by atrophy of the liver cells and secondary fibrous replacement. The firm appearance of most nutmeg livers often suggests concomitant fibrosis which can only be disproved when a microscopic examination is made. The rather widespread belief that chronic venous engorgement induces cirrhosis is chiefly based on naked-eye observation uncorrected by a further microscopic examination. Parmentier experimentally produced chronic venous engorgement of the liver in animals by setting up tricuspid regurgitation, and found that fibrosis did not follow.

In the rather exceptional instances where more fibrosis is found, some other factor, such as continued gastro-intestinal catarrh or considerable alcoholic stimulation during the course of chronic valvular disease, may be invoked. It is noteworthy that in chronic venous engorgement the resistance of the liver is necessarily reduced and that the organ is therefore more likely to be affected by poisons than in health. It would thus be reasonable to expect to find cirrhosis secondary, not to chronic venous engorgement pure and simple, but to factors such as alcoholism, auto-intoxication from intestinal fermentation (dyspeptic or Budd's cirrhosis), or actual bacterial infection. Piery, who has paid much attention to the pathogeny of so-called "cardiac cirrhosis," believes that tuberculosis and acute rheumatism may also be responsible for hepatic cirrhosis in patients with heart disease. Still, with all these different ways in which cirrhosis may become implanted on a nutmeg liver, the association of well-marked cirrhosis with chronic venous engorgement is infrequent.

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[*] Piery: Archiv général de Méd., tome clxxxvi, p. 582, 1900.
[†] Becquerel: Ibid., 1840, t. viii, p. 40.
[‡] Rokitansky: Handb. der path. Anat., 1842, Bd. iii, S. 347.
[§] Henle: Zeitsch. f. int. Med., 1844.
[‖] Budd: Diseases of the Liver, 1845, p. 118.
[**] Sabourin: Rev. de Méd., 1883, p. 523 .
[††] Handfield Jones: Med. Gaz., vol. vii, 1848, p. 1033.
[‡‡] Green: Introduction to Pathology, 1871, p. 244.
[§§] Legg, Wickham: Medico-Chirurg. Trans., vol. lviii, 1875, p. 345.

Comparison of Passive Engorgement in the Liver and Lung.—In comparing the effects of backward pressure on the liver with those on the lung it is seen that both these organs have a double blood-supply, the portal vein and the hepatic artery in the one case, and the pulmonary and bronchial arteries in the other. While pulmonary apoplexies are of frequent occurrence, the structure of the liver does not allow extensive extravasation of blood into the bile-ducts, for hæmorrhage into the bile-capillaries and ducts would constitute the exact counterpart of pulmonary apoplexies. Comparatively large areas of hæmorrhage into the liver substance occur, however, in chronic venous engorgement and can be seen microscopically to be more than engorgement. Bonome * has described hæmorrhagic infarcts in nutmeg liver.

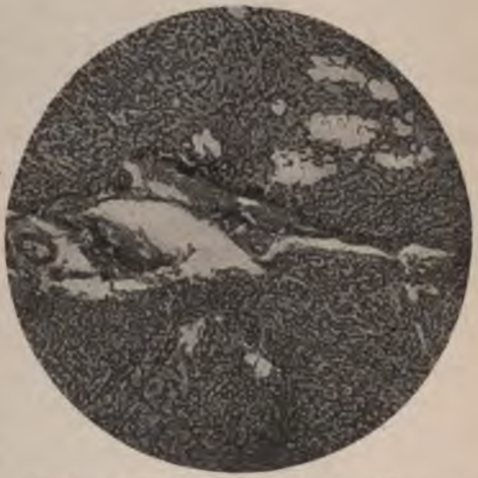

FIG. 11.—PHOTOMICROGRAPH OF LIVER IN CHRONIC VENOUS ENGORGEMENT.

Shows dilatation of capillaries and compressed liver cells. Portions of several lobules are seen. Some of the blood has fallen out of part of the section. (Photomicrograph by S. G. Penny, Esq.)

Microscopic Appearances.—The intralobular vein is dilated and its capillaries are two or three times larger than natural and full of red blood-corpuscles. This dilatation is at first limited to the central zone, but in the more advanced stages spreads into the intermediate zone towards the peripheral zone. The liver cells are compressed by the engorged capillaries and present varying degrees of distortion. Partly as the result of constant pressure, partly from impaired nutrition, due to an imperfect supply of oxygen, which necessarily follows on the stagnation of venous blood, they atrophy and may show degenerative, especially fatty, changes. The liver cells contain pigment—hæmatoidin—derived from hæmoglobin which differs from the iron-containing pigment (hæmosiderin) deposited in the peripheral zone of the lobule in pernicious anæmia, in not striking a blue colour with dilute hydrochloric acid and ferrocyanide of potassium (Perl's test). This, of course, is because hæmatoidin is iron-free.

In the peripheral part of the lobule the liver cells tend to undergo varying degrees of fatty degeneration and may contain large globules of fat. This fatty change is not, however, universally met with. In the more affected parts (the centres of the lobules) the liver cells, being compressed by the dilated capillaries, undergo atrophy and allow the vascular channels to come into contact, so that a nævoid or angiomatous appearance is produced. In these areas the blood-channels are separated

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* Bonome: Rev. général. de path. intern., 1900, p. 70.

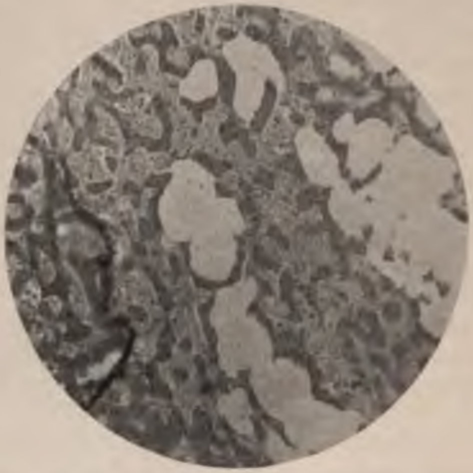

Fig. 12.—Photomicrograph of Chronic Venous Engorgement.
Same section as the foregoing; under a high power shows great dilatation of blood-capillaries and distorted liver cells. (S. G. Penny, Esq.)

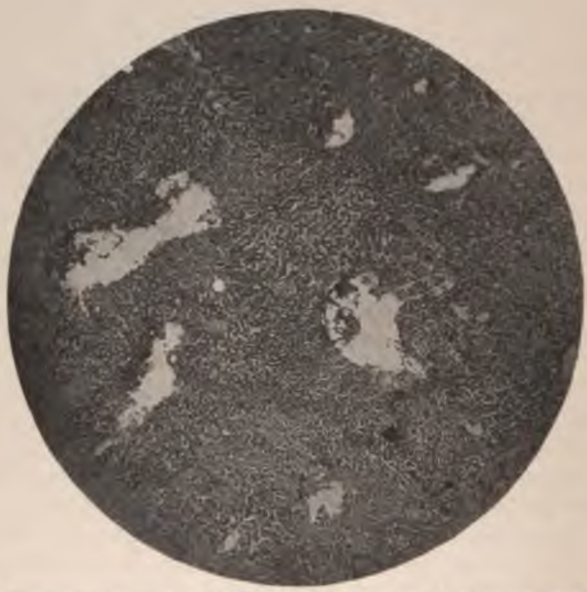

Fig. 13.—Photomicrograph of Liver showing Secondary Infiltration with Spheroidal-celled Carcinoma and Local Chronic Venous Engorgement. Low Power. (S. G. Penny, Esq.)

from each other by connective-tissue cells (Kupffer's cells). Some lobules are unaffected by the general venous engorgement, and their liver cells are either normal or hypertrophied. There may be compensatory hyperplasia,* such as is seen in a more advanced degree in nodular cirrhosis.

Jacobi† and Earl‡ have recorded cases of chronic venous engorgement of the liver in which there were multiple adenomata of liver cells, which did not show the effects of chronic venous engorgement.

The atrophy of the liver cells allows the existing fibrous tissue to become more prominent and to increase in bulk to some extent; in other words, the process of fibrous replacement. The increase in fibrous tissue is seen both around the portal spaces and also to a lesser degree in the walls of and around the intralobular veins (centrilobular cirrhosis). Its characters are sporadic or irregular distribution and absence of active hyperplasia. It is, therefore, mainly a fibrous replacement and not an active proliferation. This accounts for the apparent increase in the amount of fibrous tissue seen in a nutmeg liver. As mentioned above, nutmeg livers not infrequently have a naked-eye appearance that suggests cirrhosis, but microscopic examination shows very little fibrosis, and that of a sporadic character in no way comparable to cirrhosis. Atrophy of the liver cells and replacement fibrosis are most advanced under the capsule of the liver; macroscopically this subcapsular fibrosis closely resembles chronic perihepatitis. Microscopically, however, the capsule is seen to be unaffected. (*Vide* Fig. 15.)

The morbid anatomy of the other abdominal organs is that seen in the backward pressure of mitral or obstructive lung disease and need not be described in detail. The *spleen* is firm, deeply engorged, but not increased in weight. This is shown by Kelynack's § figures of the weight of the spleen in 56 cases of nutmeg liver due to cardiac disease and uncomplicated by any febrile or septic process, in which the average weight of the spleen was 7.3 ounces, or just about the normal. The *pancreas* may be enlarged from fibrosis and may even be palpable during life.‖ It may, however, be of normal size.**

CLINICAL PICTURE.

Symptoms.—There is a feeling of tightness, heaviness, and discomfort in the right hypochondrium, which is markedly tender on pressure. It may be noted in passing that the tenderness of an enlarged liver in alcoholic cirrhosis, which is usually explained as being due to active fibrous hyperplasia, may be due to chronic venous engorgement, the result of alcoholic dilatation of the heart. The general tenderness of a chronically engorged liver probably depends on the distension and stretching of the capsule of the organ. Very marked tenderness accompanied by pain, which is independent of palpation, is due to concomitant perihepatitis and may be accompanied by friction. Mackenzie* points out that the tenderness which is usually assumed to be in the liver is often in the abdominal walls, and that this can be shown by the fact that the area of tenderness is generally more extensive than would correspond to the liver and that the abdominal wall is tender when it is carefully lifted up.

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* Letulle: Anatomie Pathologique, vol. i, 1897.
† Jacobi, A.: Trans. Association American Physicians, vol. xii, p. 500.
‡ Earl: Lancet, 1902, vol. ii, p. 1464.
§ Kelynack: Birmingham Med. Review, Feb., 1897.
‖ Hale White: International Clinics, Series iv, p. 90, 1896–97.
** Lefas: Archiv général de Méd.: tome clxxxv, p. 539, 1900.

Chronic portal engorgement gives rise to impairment or loss of appetite, dyspepsia, flatulence, tympanites, and favours gastro-intestinal catarrh. Constipation and irregularity of the bowels with perhaps diarrhœa are part and parcel of this same condition; together they lead to considerable distension of the abdomen. The digestive disturbance, brought on by chronic venous engorgement of the liver and portal system, interferes with assimilation, and the patients are thin, though this may be somewhat masked by œdema; in children growth is interfered with and very considerable wasting may be brought about. Hæmatemesis is usually said to occur, but I have not seen it in uncomplicated cases of nutmeg liver.

In a case of mitral stenosis † with thrombosis of the splenic vein hæmatemesis occurred, but was evidently due to the extreme venous congestion of the vasa brevia of the stomach which open into the splenic vein.

Dyspnœa on exertion, and in advanced cases orthopnœa, due to the primary cardiac lesion or to concomitant ascites, are common. It is possible that dyspnœa in some instances may be due to hepatic insufficiency, and, like the uræmic form, toxæmic.

Physical Signs.—The skin over the malar bones is much congested and of a high colour, while the lips, ears, and skin elsewhere may show cyanosis. The forehead and especially the temples have a slightly icteric tint. The contrast between these two tints of the skin produces a facial aspect which is very characteristic of advanced mitral disease. The slight icteric tinge is probably due to a low grade of catarrhal inflammation of some of the small intra-hepatic bile-ducts, but it is possible that it may be mechanical and due to œdematous swelling of the mucous membrane of the bile-ducts. In some instances ordinary catarrhal jaundice depending on the spread of gastro-duodenal inflammation to the biliary papilla supervenes in the course of the disease.

The liver is nearly always enlarged, and can be felt two or three fingers' breadths below the costal arch in the right nipple line. Its size varies with, and is a fair indication of, the condition of the right side of the heart. It diminishes when backward pressure is relieved and is affected in a similar manner by free purgation. The surface of the liver is smooth to the touch and firm. When the engorgement is marked, the liver is tender from distension; the tenderness, like the increased size, is a good index of increased backward pressure. In a small percentage of cases the liver can be felt by the hand to pulsate with each beat of the heart.

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* Mackenzie, J.: The Study of the Pulse, p. 221, 1902.
† Green, T. H.: Brit. Med. Journ., 1899, vol. ii, p. 1415.

In 235 cases of tricuspid regurgitation analyzed by Pitt* pulsation was present in 15, and in 87 cases of tricuspid stenosis in 8.

When one hand is placed over the liver and the other is pressed into the right loin, the liver can be felt to expand and diminish like an accordion. This shows that the pulsation is not a transmitted impulse, but is due to the liver being injected with blood at each beat of the heart. The left lobe pulsates more than the right, as the blood regurgitates into it more readily.

Pulsation may also be communicated to the liver from a hypertrophied and labouring right ventricle, the liver receiving a jog with each beat of the heart, the left lobe being chiefly affected; in rare instances pulsation is transmitted from an abdominal or even an hepatic aneurysm.

J. Mackenzie† has made an exhaustive study of hepatic pulsation by means of the polygraph, a modification of the cardiograph. The following are some of his conclusions: Pulsation of the liver only occurs in valvular disease, but is very commonly detected by this instrument, though not by the hands. When once the liver has begun to pulsate, it probably always continues to do so till death. Pulsation of the liver may be synchronous with the systole of the ventricles or of the auricles, and corresponds with the rhythm of venous pulsation in the neck. Pulsation of the liver synchronous with contraction of the auricle is generally associated with tricuspid stenosis and may be confused with pulsation communicated to the liver from a vigorously contracting heart.

If pressure in an upward direction is made on the liver, the jugular veins in the neck may be observed to swell up. The incompetency of the valves at the origin of the jugular veins allows the column of blood in the inferior vena cava, right auricle, and superior vena cava to be displaced upwards.

The enlarged liver may push the diaphragm up and by encroaching on the thorax lead to some collapse of the base of the right lung. Dulness, absence of breath-sounds and of vocal vibrations at the base of the right lung behind are not uncommon in cases of advanced mitral disease, and may be due to collapse of the lower lobe of the lung or to a pleural effusion.

Chronic venous engorgement of the liver necessitates chronic portal obstruction; ascites may thus be set up, and if of long duration is found to be associated with a certain amount of chronic peritonitis. Whether the latter is set up by the ascites or whether the ascites is the result of the chronic peritonitis brought about by chronic portal and peritoneal engorgement is open to discussion. Probably most observers would consider the chronic peritonitis the primary and important factor. Ascites occurs in more than half the cases of tricuspid regurgitation, but is less frequent than œdema of the feet.

Thus, in 235 cases of tricuspid reflux collected by Pitt,‡ œdema was noted in 200 and ascites in 140. So far as these figures go it might appear that ascites is only part of an ascending œdema. Dr. Pitt has kindly provided me with a further analysis which showed that œdema and ascites occurred together in 124 cases, œdema alone in 76, ascites alone in only 14, and neither in 21. This tends to support the view that the ascites of nutmeg liver is part of a general œdema.

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* Pitt, G. N.: Allbutt's System of Medicine, vol. vi, p. 16.
† Mackenzie: A Study of the Pulse, p. 220, 1902.
‡ Pitt, G. N.: Allbutt's System of Medicine, vol. vi, p. 16.

This form of ascites resembles that of chronic peritonitis in persisting and recurring, and in not being, like the ascites of cirrhosis, a close forerunner of death. The fluid is straw-coloured, as a rule, but has been known to be chyliform.

Dry pleurisy may occur or signs of pleural effusion at the right base; these may be explained as the result of pulmonary apoplexy, which is commoner in the lower lobe of the right lung. On the other hand, the upward pressure of the enlarged liver may simulate closely a small effusion.

The Urine.—The amount of urine is diminished from chronic venous engorgement of the kidneys, but as the result of treatment with digitalis and other cardiac tonics, the amount of urine may be far above the normal for a time. In cases where chronic venous engorgement of the liver is marked the urine is concentrated, of a high specific gravity, high coloured, and on cooling deposits urates. It contains urobilin and in some instances hæmatoporphyrin,* but unless there is definite jaundice bile-pigment is usually absent. In some instances there is albuminuria; its occurrence is variable and does not necessarily depend on gross structural change. In cases where backward pressure falls on the renal veins in a marked degree the nutrition of the renal epithelium may be sufficiently impaired to allow of albuminuria. Alimentary glycosuria is quite exceptional and probably depends on concomitant pancreatic change rather than on hepatic insufficiency. The excretion of urea varies with the amount of urine; diminution in its amount has been correlated with hepatic insufficiency.

There is delay in absorption of liquid from the intestines, and accordingly the amount of urine excreted during digestion, instead of being larger than that excreted during fasting, the normal relationship, is less (Gilbert and Lereboullet†). This has been tested by giving meals with eight-hour intervals and collecting the urine every four hours. The term *opsiuria* has been applied to this condition (Lecerf‡).

Complications.—Well-marked jaundice may be produced by extension of catarrhal gastritis to the duodenum, and so to the biliary papilla and lower end of the common bile-duct. In rare instances jaundice may be a terminal event due to acute infection falling on the liver and setting up icterus gravis.

In chronic venous congestion of the liver there are several factors favouring the development of auto-intoxication.

(I) In the liver itself. Owing to malnutrition the antitoxic or poison-stopping function of the liver cells is impaired or arrested. Toxic bodies derived from the alimentary canal therefore tend to pass into the general circulation and affect the nervous centres.

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* Garrod, A. E.: Lancet, 1900, vol. ii, p. 1327.
† Gilbert and Lereboullet: Soc. de biolog., Paris, Mar. 9, 1901.
‡ Lecerf: Thèse, Paris, 1901.

(II) Owing to portal stagnation the processes of digestion are interfered with and more toxic material is carried to the liver, which is, as has already been said, unable to cope with even the normal amount.

(III) Chronic venous engorgement of the renal veins leads to diminished urinary excretion.

Course.—The course of the disease depends on the condition of the heart, and may, like it, improve periodically only to relapse again. The hepatic enlargement tends to increase during each recurrence, though, as already pointed out, the liver gets somewhat atrophied towards the end of a case. According to Mackenzie, pulsation when it appears remains to the end.

Termination.—Death is commonly due to gradually increasing cardiac failure or to some terminal or secondary infection, usually of other parts of the body, such as pneumonia, pleurisy, etc. The infection, however, may attack the liver itself, and thus give rise to icterus gravis either with a high or with a low temperature. In such cases diarrhœa and vomiting are the early symptoms; jaundice, hæmorrhages, and dry tongue develop and finally coma precedes death. A slighter degree of the terminal infection may show itself by acute perihepatitis.

DIAGNOSIS.

When the cardiac lesion is manifest, there will be no difficulty; but in the class of cases termed by Hanot hepatic asystole, where attention is focused on the liver, the condition may appear to be primarily hepatic and be thought to be cirrhosis, or, when the liver is large and very tender, malignant disease.

With regard to the diagnosis from cirrhosis, it is noteworthy that the abdominal wall does not show the dilated veins seen in many cases of hepatic cirrhosis, and that there is no enlargement of the spleen, while the symptoms improve on cardiac tonics. Examination of the heart and lungs should always be made in any case of cirrhosis, and the existence of definite signs of mitral disease should lead to revision of the diagnosis; but an apical systolic murmur is not infrequent in cirrhosis, though it is seldom persistent. In cases of hepatic asystole the history, the smooth surface of the liver, the comparatively smaller amount of enlargement, and diminution in size following cardiac tonics, together with absence of severe pain and of cachexia, should enable the observer to eliminate malignant disease.

TREATMENT.

Treatment may be divided into two heads, which, however, overlap to a certain extent. The first and most important is that of the primary heart disease or of the combined lung and heart affections. Digitalis is the most efficacious drug and may be given as the tincture in x to xv minim doses three or four times a day, or the fresh infusion in drachm doses. Digitalin is not so efficacious as the tincture or infusion. The pill containing digitalis, squills, and mercury (Addison's pill at Guy's

Hospital, Baillie's pill at St. George's) is often very successful. Digitalis with citrate of caffeine may also be given. Strophanthus, though well adapted for mitral stenosis, and convallaria, are not so powerful for good in tricuspid reflux as digitalis. If there be emphysema and bronchitis, iodide of potassium, carbonate of ammonia, ipecacuanha, may be given in addition. Rest in bed, and if necessary paracentesis of the abdomen or tapping of the legs, are essential parts of the treatment.

In the second place, the engorgement of the liver and its results may be further treated by purgatives, diuretics, and local applications. As purgatives, magnesium sulphate or sodium sulphate should be employed to run off the excess of fluid from the intestinal vessels; mercury in the form of blue pill or calomel is a valuable remedy. Aloes and l'eau de Vie allemande may also be given with advantage. As diuretics the cardiac tonics already mentioned and apocynum may be employed.

The administration of liver substance by the mouth is said* to act as a diuretic when the lesion is not too advanced and to increase the amount of urea and diminish the abnormal constituents, such as urobilin and albumin, present in the urine.

If there be much pain and perihepatitis is present, poultices, hot applications, leeches over the liver, or bleeding may be employed. The diet should be simple, nutritious, and not mainly as liquid, as this tends to aggravate the already waterlogged condition of the patient. For sleeplessness morphia is the most satisfactory drug; sulphonal or preferablytrional, which acts more rapidly, chloralamide, or paraldehyde may also be tried, but should not be given constantly; if a sleeping draught is frequently needed, its composition should be changed. Spa treatment at Vichy, Neuenahr, Nauheim, Pougues, etc., may be tried when the patient is sufficiently well to bear the journey.

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* Spillmann and Dernange: Congrès de Med. Int., Lille, 1899.

PERICARDITIC PSEUDO-CIRRHOSIS OF THE LIVER.

This condition, which for practical purposes may be regarded as an extreme grade of chronic venous engorgement of the liver in cardiac patients with adherent pericardium, was described by Pick * in 1896. The clinical features—recurrent ascites, an enlarged firm liver, absent or slight jaundice, and no œdema of the legs—may suggest cirrhosis, inasmuch as during life adherent pericardium may be latent or may be overlooked. The liver is in an extreme stage of chronic venous engorgement and shows fibrous hyperplasia. Any peritoneal adhesions or thickening that may be present were regarded by Pick as accidental or secondary either to chronic venous engorgement of the peritoneum or to ascites. Cases of this kind chiefly occur in young subjects with a history of rheumatic endocarditis and pericarditis and without any of the usual antecedents of hepatic cirrhosis.

This condition merges, on the one hand, into chronic venous engorgement of the liver, with which it is, to my mind, most closely allied; and, on the other, into cases of universal perihepatitis associated with adherent pericardium (*vide* p. 164). Some few adhesions or slight peritoneal thickenings are comparatively frequent in the cases belonging to the group described by Pick; when these peritoneal changes are advanced, the condition ceases to be Pick's pseudo-cirrhosis of pericardiac origin and belongs to that of chronic universal perihepatitis associated with adherent pericardium (multiple serositis). Kelly † groups together under the heading of multiple serositis these cases of Pick's pseudo-cirrhosis and the cases of "iced liver," or, as they are usually called in England, "chronic universal perihepatitis." To quote his own words: "Some distinction—anatomically at least—may be drawn between cases in which the lesions are confined to the peritoneum and cases in which the lesions are more widespread. The cases in which the pericardium is unaffected reveal no congestive alterations in the liver. Clinically, however, the two classes of cases are very much alike, and the 'Zuckergussleber' may occur in both."

The following case, in which there was some chronic peritonitis, otherwise exactly resembled Pick's pseudo-cirrhosis, but from the presence of peritoneal change it must be regarded as occupying a position midway between pseudo-cirrhosis and chronic peritonitis associated with adherent pericardium (multiple serositis).

A girl aged four was under my care in St. George's Hospital with recurrent ascites, chronic jaundice of slight degree, a large pulsating liver, and pulsating jugular veins more marked on the right side of the neck. The heart was much enlarged, there were systolic and diastolic apical murmurs, and an accentuated pulmonary second

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* Pick: Zeitschrift f. klin. Med., Bd. xxix, S. 385.

† Kelly, A. O. J.: American Journ. of Med. Sciences, vol. cxxv, p. 116.

sound. At the autopsy the pericardium was universally adherent, the left ventricle was dilated, greatly hypertrophied, and showed much chronic endocarditis of the musculi papillares. The mitral valve segments were much thickened and the orifice was somewhat dilated. The left auricle was also dilated. The right side of the heart, contrary to what was expected, was not dilated. The heart and pericardium weighed 17 ounces. The hepatic veins were enormously dilated and were each of them as large as the inferior vena cava. The liver was nutmeggy and showed scattered adhesions to the diaphragm. Microscopically the appearances were the same as those seen in figures 14, 15, viz., sporadic and subcapsular fibrosis and extreme chronic venous engorgement. There were a few adhesions and a few ounces of fluid in each of the pleuræ and general opacity of the peritoneum.

Eisenmenger,* who among others disputes the existence of the condition as a distinct morbid entity, believes that in children the vessels of the general systemic circulation have a better tone and are less disposed to allow transudation to occur than in older people, and that the more marked hepatic manifestations are thus accounted for. He further puts forward the suggestion that adhesions in connexion with the adherent pericardium, or a concomitant pleural effusion may lead to torsion of the inferior vena cava close to the diaphragm and so lead to ascites; while in other instances local peritonitis in the portal fissure may be the real cause of ascites.

MORBID ANATOMY.

The liver often shows some scattered adhesions to the diaphragm. Its general appearance is that of advanced chronic venous engorgement. There is no general chronic peritonitis or universal perihepatitis, but the surface of the liver is usually somewhat irregular, as in ordinary chronic venous engorgement, and often opaque. This opacity is due to fibrosis under the capsule, due to fibrous replacement, and on superficial examination resembles chronic perihepatitis, for which it has probably often been taken. On section the liver shows advanced chronic venous engorgement.

Microscopic Appearances.—The liver shows marked chronic venous engorgement with very irregularly scattered islands of fibrosis. Much of this apparent increase in the amount of fibrous tissue is due to atrophy of the liver cells allowing the existing fibrous tissue to come into prominence. There is perhaps a little active proliferation or fibrous hyperplasia, and, by careful selection, areas resembling multilobular cirrhosis with the addition of chronic venous engorgement can be found in microscopic sections. Taken as a whole, however, the amount of fibrosis is scanty, and may be absent in considerable areas.

Under the capsule there are extensive atrophy of the liver cells and fibrous replacement. If microscopic examination was limited to a section from this part of the liver, there would appear to be extremely marked fibrosis. But the extent of the fibrous change is limited to a small area under the capsule. It is, however, enough to produce very definite opacity, and, as has already been pointed out, imitates universal chronic perihepatitis. The two conditions are entirely different: in chronic universal perihepatitis ("Zuckergussleber," "iced liver") the fibrosis is on the outer surface of the capsule. The appearances in subcapsular fibrosis are well shown in the accompanying drawing (Fig. 15), taken from a case of this kind.

The liver thus shows the changes of chronic venous engorgement with rather more sporadic fibrosis than is usually present, but there is no

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* V. Eisenmenger: Wien. klin. Wochen., Bd. xiii, 1900.

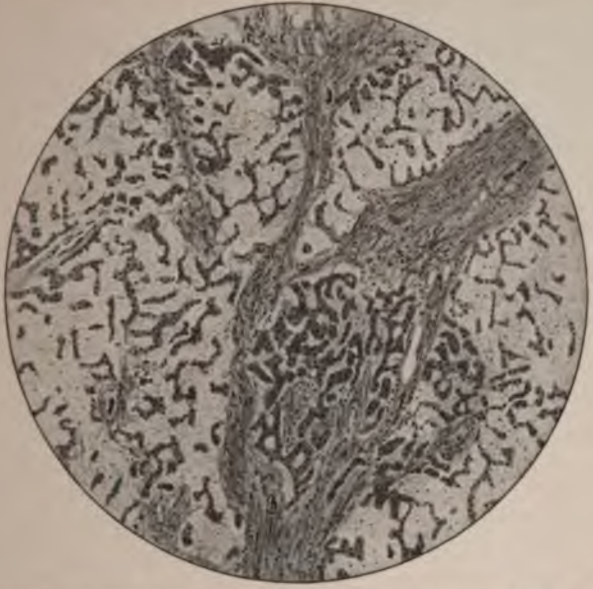

FIG. 14.—MICROSCOPIC SECTION FROM AN ADVANCED CASE OF NUTMEG LIVER ASSOCIATED WITH ADHERENT PERICARDIUM. (Case on p. 97.)

The blood-capillaries are enormously dilated, the liver cells are compressed and distorted, and there is sporadic fibrosis. This section was specially chosen so as to show "cardiac fibrosis." × 60.

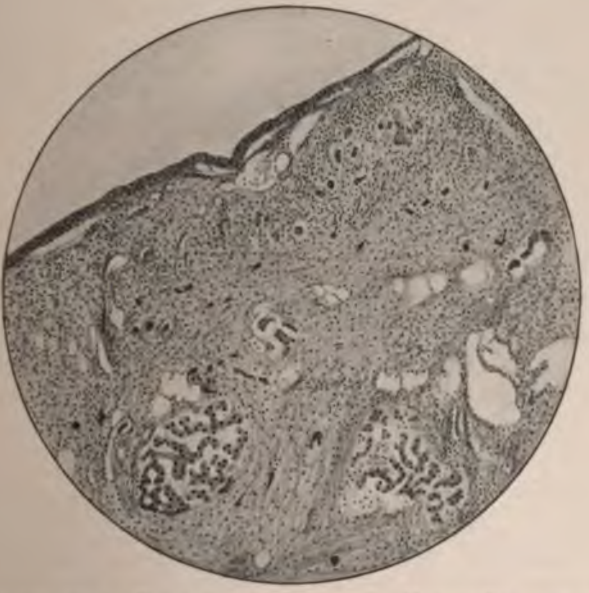

FIG. 15.—DRAWING FROM A MICROSCOPIC SECTION SHOWING MARKED SUBCAPSULAR FIBROSIS. The real capsule is seen on the free surface. (From the same case as figure 14.)

tendency to compression or narrowing of the branches of the portal vein, as in genuine portal cirrhosis. Although there is, as a rule, no genuine cirrhosis comparable to portal cirrhosis, in cases of ordinary adherent pericardium it appears from Diemar's [*] and Wells' [†] figures that when calcification occurs in an adherent pericardium well-marked hepatic cirrhosis is found in the great majority of cases. What relationship, if any, exists between calcified pericardium and hepatic cirrhosis is unknown. These cases occur in adults, while the patients with Pick's pseudo-cirrhosis are usually children. I have examined some of these cases, expecting to find an extension of fibrosis from the adherent pericardium along the hepatic veins into the substance of the liver, but have never found any fibrosis, though the inner walls of the hepatic veins and inferior vena cava are opaque and thickened, as is commonly seen in cases of backward pressure. The pericardium is firmly adherent to the heart, and usually to the chest wall as well. These adhesions are usually due to past rheumatic pericarditis, but in some instances the pericarditis is tuberculous, and under these conditions the liver may also be tuberculous.

Mechanism of the Morbid Processes.—The pericardial adhesions by contracting lead to dilatation of the right auricle, inferior vena cava, and hepatic veins, and by this means the free regurgitation of blood into the liver is rendered permanent. It is possible that at the time of the primary pericarditis inflammation spreads to the mouths of the hepatic veins, and by weakening their walls leads to dilatation and so to a freer entry of blood into them. When once brought about, this dilatation of the hepatic veins probably becomes permanent. The brunt of backward pressure thus falls on the liver, while the other branches of the inferior vena cava—the renal and iliac veins—suffer less than in ordinary cases of chronic engorgement of cardiac origin.

The *clinical aspect* of the cases has already been referred to, and the absence of œdema of the legs, which may tend to differentiate the condition from ordinary backward pressure of heart disease, has been mentioned. During life the liver may be firm and enlarged, and so may suggest cirrhosis, especially if the presence of an adherent pericardium be overlooked and the signs and symptoms of valvular disease are not prominent. In most instances the associated cardiac and pericardial disease will be easily detected and no doubt will arise. In these cases it may be necessary to tap the abdomen on a considerable number of occasions, but the intervals are often prolonged, thus differing from the frequent paracenteses necessary in chronic peritonitis. Jaundice is either absent or slight. The following case illustrates the general features of the condition:

Girl aged eleven years was under the care of my colleague, Dr. Penrose, for three years with morbis cordis and ascites, for which tapping had been required about fifteen times. At the autopsy there was mitral and tricuspid incompetence with an adherent pericardium; the liver—3 pounds 6 ounces—was enlarged and showed some thickening of its capsule with a few adhesions. The hepatic veins were very prominent but there was no fibrosis around them. The surface of the liver was irregular from depressed lines due to atrophy and fibrous increase around the subcapsular veins. On section the liver was nutmeggy and gave the impression of some fibrous increase. Microscopically there was sporadic fibrosis, but no genuine multilobular cirrhosis, the branches of the hepatic veins and intralobular venules were greatly dilated, and the liver cells atrophied. The appearances were those of advanced chronic venous engorgement with more fibrosis than usual. There was no chronic peritonitis; there were old adhesions in the left pleura and recent ones in the right pleura.

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[*] Diemar: Zeitsch. f. Heilk., 1899, Bd. xx, S. 257.

[†] Wells, H. G.: American Journ. of Med. Sciences, vol. cxxiii, p. 259, 1902.

PROGNOSIS AND RESULTS.

When the condition of hepatic pseudo-cirrhosis has become established the prognosis is very bad, though life may be prolonged for a considerable time. Tuberculous peritonitis may supervene as a secondary result; this was proved to be the sequence of events in a case recorded by Nachod,* where laparotomy a year before death proved the absence of tubercle at that time. Secondary tuberculous infiltration of the portal spaces may then occur. The term cardio-tuberculous cirrhosis has been applied to advanced chronic venous engorgement of the liver complicated in this way by tuberculous infection.† These cases, which are chiefly met with in children, are associated with more advanced tuberculous disease elsewhere, especially in the peritoneum and pleura.

These conditions of "hepatic pseudo-cirrhosis" and cardio-tuberculous cirrhosis are closely allied both to nutmeg liver and to the cases of general perihepatitis secondary to adherent pericardium. Clinically the chief difference from nutmeg liver is the absence of any signs of cardiac valvular disease. The proper treatment, however, is that of chronic venous engorgement of the liver, viz., cardiac tonics and diuretics. The treatment suitable for cirrhosis is of no use in these conditions.

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* Nachod: Prag. med. Wochenschrift, 1898, S. 330.

† *Vide* Moizard and Phulpin: Archiv. de Médicine des Infants, Aug.: 1899. Cousin: Gaz. hebd. de Méd. et de Chirurg., Jan. 14, 1900. Wells, H. G.: American Jour. Med. Sciences, vol. cxxiii, p. 299.

INFARCTS IN THE LIVER.

Infarcts are usually considered to be rare in the liver. Contrary to what might be supposed from the fact that the liver has a double blood-supply, from the hepatic artery and portal vein, appearances resembling infarcts in other organs do occur in the liver and are not so rare as is usually believed.

Infarcts in the liver usually show some differences from those in the spleen and kidney which have true end-arteries.

(1) They are generally hæmorrhagic, whereas bland infarcts in the kidney and spleen are usually anæmic. The hæmorrhagic state of the hepatic infarcts is doubtless due to the double blood-supply, and in this way infarcts of the liver and lung, both of them organs with a double blood-supply, resemble each other.

(2) Necrosis and coagulation necrosis seldom occur, inasmuch as the nutrition of the liver cells is maintained by the collateral circulation.

(3) As there is usually no necrosis, fibrous substitution seldom occurs to more than a slight extent, and it is doubtful whether a depressed scar on the site of the infarct is ever produced.

It might perhaps be thought convenient to make some distinction between the infarcts in the liver and those in the spleen and kidney. The term pseudo-infarcts is open to objection as being a contradiction in terms. Professor Adami has suggested in a letter to me that the term subinfarct might be employed to indicate a condition approaching but not exactly the same as an infarct in the spleen and kidneys. This term would also be of use in distinguishing between true anæmic infarcts of the liver (as Baldwin's case [*]) with necrosis and the hæmorrhagic subinfarcts in which necrosis of the liver cells does not occur.

Infarcts in the liver may be either hæmorrhagic or anæmic. The hæmorrhagic variety is more frequent.

In 32 cases collected by Lazarus-Barlow,[†] including Chiari's [‡] 17 cases, 28 were hæmorrhagic and four anæmic. In 40 cases, including most of Lazarus-Barlow's, 29 were hæmorrhagic, 10 were anæmic, and in one case of Pitt's [§] both hæmorrhagic and anæmic infarcts were present.

MORBID ANATOMY.

Hæmorrhagic infarcts in the liver are well-defined areas, sometimes square or pyramidal. In their general appearance they resemble hepatic nævi, but they are, as a rule, much larger. They are not raised above the surrounding surface of the liver; in fact, Zahn has spoken of them as

[*] Baldwin, F. A.: Journ. Medical Research, vol. viii, p. 431.

[†] Lazarus-Barlow, W. S.: Brit. Med. Jour., 1899, vol. ii, p. 1342.

[‡] Chiari: Zeitschrift f. Heilkunde, Bd. xix, S. 475.

[§] Pitt, G. N.: Trans. Path. Soc., vol. xlvi, p. 75.

atrophic hæmorrhagic infarcts. Histologically the liver cells are atrophied, granular, and may contain fat globules, while the nuclei do not stain well. There is, however, no coagulation necrosis. The capillaries are engorged with blood. There may be a considerable number of leucocytes infiltrating the affected area.

In Anæmic Infarcts.—The affected area of the liver is of a whitish-yellow colour and is sharply marked off from the surrounding healthy liver substance. There may be, but is not necessarily, a zone of congestion immediately at the junction of the infarct and the healthy liver tissue.

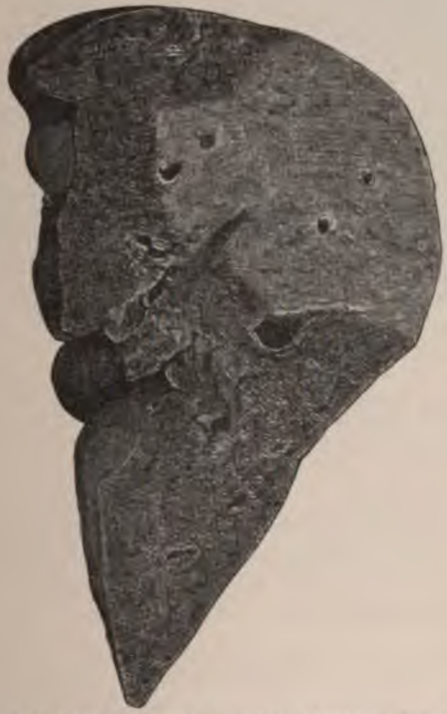

FIG. 16.—ANÆMIC INFARCT IN THE LIVER FROM A CASE WHERE THERE WAS THROMBOSIS OF THE INTRAHEPATIC BRANCHES OF THE PORTAL VEIN AND AN EMPYEMA. (Drawn by L. Jones, M.B., F.R.C.S.)

The infarct has much the same appearance, only it is larger and more prominent, as the white patches seen on the surface of the liver in many infectious diseases which on microscopic examination show local fatty change. Microscopically in an anæmic infarct the capillaries are empty instead of being engorged as in a hæmorrhagic infarct. The liver cells are atrophied and degenerated. Baldwin * described necrosis of the cells and laid stress on this observation as showing that the condition was the same as anæmic infarcts in other organs. At the margin of the infarct there are a number of leucocytes, red blood-corpuscles, and altered blood-pigment.

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* Baldwin: Journ. Med. Research, vol. viii, 431.

As a result of infarction a slight amount of localized replacement fibrosis may result, but probably not enough to give rise to a cicatrix. Frerichs * described depressed areas of atrophy on the surface of the liver, producing lobulation, as due to thrombosis of branches of the portal vein; it is conceivable that in their earliest stages these areas were infarcts. Infarct of the liver cannot be recognized clinically and is only of pathological interest.

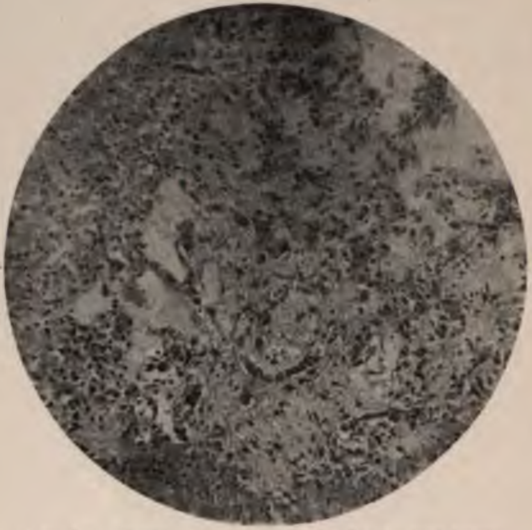

FIG. 17.—PHOTOMICROGRAPH OF INFARCT IN THE LIVER.
In part of the section the liver cells have lost their outline and their nuclei only remain. (S. G. Penny, Esq.)

ETIOLOGY.

. The conditions which have been thought to play a part in producing infarction of the liver are:

1. Obstruction of the branches of the portal vein, either by embolism or thrombosis.
2. Obstruction of the branches of the portal or hepatic veins by new-growth.
3. Obstruction of both the portal and hepatic veins at the same time.
4. Embolism of the hepatic artery.
5. Endarteritis of the hepatic artery.
6. Retrograde embolism of the hepatic veins.
7. Severe traumatism.

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* Frerichs: Diseases of the Liver, vol. ii, p. 396. Translated by New Sydenham Soc.

(1) **Embolism and Thrombosis of the Branches of the Portal Vein.**—The most frequent vascular lesion found in cases of infarcts in the liver is the presence of antemortem blood-clot in the intra-hepatic branches of the portal vein, either embolic and conveyed from thrombosis in its tributaries, or formed *in situ*.

Embolism.—Chiari records 15 cases of hæmorrhagic infarcts in the liver due to embolism. This number is comparatively large and rather contrasts with the isolated observations of others, which, though less numerous, point to thrombosis of the vein as a more frequent antecedent. Chiari's cases, however, include embolism with fragments of new-growth as well as with detached blood-clot.

Thrombosis.—Thrombosis of branches of the portal vein, without any other vascular obstruction, such as embolism of the hepatic artery or thrombosis of the hepatic veins, has been found in cases of hepatic infarction by Osler,* Pitt,† Chiari,‡ and others. I have certainly seen this association on three occasions. As examples of hepatic infarcts due to, or at least associated with, thrombosis in the intra-hepatic branches of the portal vein the following cases may be quoted:

A man aged forty-six, under the care of Dr. Penrose, died on May 3, 1902, in St. George's Hospital with a right-sided empyema and a dilated heart; there had been no abdominal symptoms and no ascites. The main trunk of the portal vein had an adherent parietal thrombus, and some of the branches of the portal vein in the right lobe of the liver were occluded with firm clots. There were two anæmic infarcts, one as large as one's hand, the other a quarter of that size. The veins going to these areas were thrombosed. The hepatic artery was opened up and was found to be free from embolism, thrombosis, or arteriosclerosis. The infarcted areas were distinctly raised above the level of the surrounding liver substance. Although the macroscopic appearances were those of an anæmic infarct, the microscopic were those of a hæmorrhagic infarct, the capillaries being full of blood. It is possible that in this case backward pressure from the dilated heart and sepsis played some part in addition to portal thrombosis in inducing the infarctions.

A man aged forty-eight under the care of Sir. W. Bennett and myself was operated upon for a localized subphrenic abscess due to a perforated gastric ulcer. Thrombosis of the right popliteal vein developed before death, and at the autopsy thrombosis of a branch of the right division of the portal vein with a sharply marked hæmorrhagic area was found in the corresponding part of the liver.

(2) **Obstruction of Branches of the Portal and Hepatic Veins in the Substance of the Liver by New-growth.**—Both these conditions may be associated with infarction of the liver. When the intra-hepatic branches of the portal vein are obstructed by growth the process is usually embolic and due to small emboli of infective cells derived from a carcinoma in the stomach, colon, or other organs within the territory of its tributaries. When the hepatic veins are occluded, the growth may involve them from without, spread through the capillaries from embolic growths in the portal vein, or in rare cases be due to retrograde embolism. (*Vide* p. 51.)

In a woman aged forty who died in St. George's Hospital with a spindle-celled sarcoma surrounding the pancreas there were secondary growths in the liver which blocked up some branches of the hepatic veins and gave rise to hæmorrhagic infarcts in the corresponding areas. There were anæmic infarcts in the spleen due to blocking of the splenic vein. There was no evidence of arterial embolism. Longcope* describes an anæmic infarct associated with thrombosis of the hepatic vein, and a hæmorrhagic infarct associated with thrombosis of the portal vein; in both Longcope's cases the thromboses were secondary to gastric carcinoma.

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* Osler: Trans. Assoc. American Physicians, vol. ii, p. 136, 1887.

† Pitt: Trans. Path. Soc., vol. xlvi, p. 75.

‡ Chiari: Zeitschrift f. Heilkunde, Bd. xix, S. 475.

(3) **Combined Portal and Hepatic Vein Thrombosis.**—Thrombosis of the portal vein may, when combined with thrombosis of the hepatic veins, give rise to infarction of the liver. Thus, Pitt † records a case of very widespread thrombosis in the abdominal aorta, splenic, left renal, and right middle cerebral arteries, in the right hepatic and the branches of the portal veins. There were both anæmic and hæmorrhagic infarcts in the liver. But in a case of combined hepatic and portal vein thrombosis that I examined there was no appearance of infarction in the liver.‡

(4) **Embolism of the hepatic artery** is very rare. It has been found both in man and experimentally to lead to necrosis of the liver. (*Vide* p. 45.) Embolism of its branches may give rise to anæmic infarcts.

In a case of embolism of the bifurcation of the hepatic artery by a vegetation derived from the aortic valves C. Ogle § found anæmic infarcts in the liver.

In a case of aortic and mitral disease Baldwin ‖ found between 20 and 30 anæmic infarcts in the liver which were genuinely necrotic. The corresponding branches of the hepatic artery contained old thrombi. There were infarcts in the spleen, kidneys, brain; so there is little doubt that the infarcts in the liver were embolic.

It is highly probable than in some cases there is embolism of the intra-hepatic branch of the hepatic artery going to the infarcted area in the liver, but that it is not found; in the following case this hypothesis is quite conceivable.

In a man aged fifty-three years who died in St. George's Hospital in November, 1902, with an abscess and pneumonia of the right lung, there was a hæmorrhagic infarct in the liver; the portal vein and hepatic artery appeared normal.

(5) **Endarteritis obliterans** of the branches of the hepatic artery has been described by Bonome ** as the cause of hæmorrhagic and of necrotic infarcts in the liver in cases of cirrhosis.

(6) **Retrograde Embolism.**—Embolism of one of the hepatic veins by a clot derived from the heart which had worked its way against the flow of blood—or retrograde embolism—has been observed to be associated with an hepatic infarct. (Arnold.††)

(7) **Traumatism** may lead to the production of appearances resembling infarcts in the liver. But these appearances are in reality different both in their minute structure and causation from the infarcts already described.

Appearances Resembling a Hæmorrhagic Infarct.—In rare instances traumatism may lead to the passage of part of the liver through a hole or rupture in the diaphragm. If the piece of liver becomes strangulated, hæmorrhage takes place into the liver and the appearance resembles that of a hæmorrhagic infarct.

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* Longcope, W. T.: University of Pennsylvania Med. Bull., Aug., 1901, p. 223.

† Pitt: Trans. Path. Soc., vol. xlvi, p. 75.

‡ Rolleston: Trans. Path. Soc., vol. l, p. 148.

§ Ogle, C.: Trans. Path. Soc., vol. xlvi, p. 73.

‖ Baldwin, F. A.: Journ. of Medical Research, vol. viii, p. 431.

** Bonome: Lo Sperimentale, anno 53, fasc. 4, p. 319. Rev. général de Path. Intern. 1900, p. 70.

†† Arnold: Virchow's Archiv, Bd. cxxiv, S. 388.

In a remarkable case recorded by C. Ogle,[*] part of the left lobe of the liver, measuring 5 by 4 inches, was herniated through the diaphragm, and to the naked eye resembled a section of a cardiac spleen. Microscopically the liver tissue was disorganized and showed much blood pigment, red blood-corpuscles, and the remains of liver cells, but differed considerably from the appearances in an ordinary hæmorrhagic infarct of the organ. I had an opportunity of cutting sections of the specimen.

Anæmic Infarcts.—Severe traumatism may, by producing rupture of the liver, cut off the vascular supply to a part or parts of the liver. If life is prolonged for some days, the areas of the liver thus deprived of their blood-supply present to the naked eye an appearance resembling an anæmic infarct. The areas are firm and white in colour and have been regarded as infarcts by Klebs,[†] Lubarsch,[‡] Lazarus-Barlow,[§] Heile.[||] Microscopic examination shows that there is undoubted necrosis in these areas and that they correspond to true infarcts in the kidney and spleen. There is therefore a distinct difference between them and the so-called infarcts of the liver previously described, with the exception of Baldwin's.

(8) There may be no manifest vascular obstruction to be found. In such cases a septicæmic or toxæmic condition is possibly responsible for the lesion. I have seen an infarct in the liver without any evidence of portal thrombosis or embolism of the hepatic artery. The patient was a man aged twenty-five who died with a localized peritonitis in the lesser sac due to acute pancreatitis.

PATHOLOGY.

Experimentally Cohnheim and Litten[**] injected coarsely powdered chromate of lead and wax into the portal vein and produced portal thrombosis but no infarcts. Zahn,[††] however, is quoted by Welch to the effect that sterilized mercury injected into the mesenteric veins was followed after an interval of eight days by hæmorrhagic infarcts. But in actual practice thrombosis of the portal vein or its branches is so frequently seen without any accompanying infarction that it would appear that some other factor is necessary. Rattone suggested that the additional factor is blocking of the hepatic artery, but this is hardly ever found to be the case; Chiari argued in favor of a feeble circulation and low blood-pressure in the hepatic artery associated with venous congestion. Kohler[‡‡] thought that backward pressure in the hepatic veins was a necessary adjunct, but this, again, is not borne out by the facts of morbid anatomy. It is probable, therefore, that infarction of the liver is not solely a mechanical process.

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[*] Ogle, C.: Trans. Path. Soc., vol. xlviii, p. 114.
[†] Klebs: Virchow's Festschrift, 1891, S. 8.
[‡] Lubarsch: Fortschritte d. Med., 1893.
[§] Lazarus-Barlow: Brit. Med. Journ., 1900, vol. ii, p. 1362.
[||] Heile: Ziegler's Beiträge, Bd. xxviii, S. 443, 1900.
[**] Cohnheim and Litten: Virchow's Archiv, Bd. lxvii, S. 153.
[††] Zahn: Centralblatt f. allg. Path., viii, S. 860, 1897.
[‡‡] Kohler: Quoted by Welch, Allbutt's System, vol. vi, p. 280.

By the injection of tissue fibrinogen Wooldridge * produced portal thrombosis with hæmorrhages and necrotic areas in the liver. The necrosis is a more advanced change than that seen in the ordinary so-called infarcts in the liver. Wooldridge's results suggest that, in addition to vascular disturbances, such as thrombosis or embolism of the blood-vessels of the liver, a toxæmic or septicæmic condition is necessary or at least very favourable to the production of infarction in the liver. Possibly a low arterial blood-pressure, which is favoured by septicæmia, may, when combined with a septic or toxic blood state, be sufficient to produce hepatic infarction. The importance of a septic condition is supported by the fact that Apert † produced multiple anæmic infarcts, resembling the early stage of abscess formation, in the liver, heart, and kidneys of a rabbit by injecting pus containing colon and numerous anaërobic micro-organisms into the vein of the ear.

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* Wooldridge, L. C.: Trans. Path. Soc., vol. xxxix, p. 421.

† Apert: Bull. Soc. Anat. Paris, 1900, tome ii, p. 204.

ACUTE CONGESTION OF THE LIVER.

Active acute congestion of the liver is, of course, the first stage of acute hepatitis, which may, like similar processes elsewhere, abort and be followed by a rapid return to the normal condition. It is therefore impossible to draw a hard and fast line between the clinical manifestations of active congestion and of acute hepatitis in an early stage. Acute congestion of the liver is both more frequent and of more importance in warm countries, where malaria and dysentery are rife, than in temperate countries.

From a systematic standpoint the causes of active congestion of the liver may be first divided into:

(I) Active vaso-dilatation of the capillaries of the hepatic artery; this may be reflex and due to the effects of cold applied to the surface of the body. This is the mechanism by which chills produce active congestion of the liver. In England cold does not act in this way to anything like the same extent that it does in tropical climates, where the resistance of the liver is often much diminished from past attacks of congestion or inflammation in connexion with malaria and dysentery. In persons who have had dysentery or repeated attacks of malaria exposure to cold readily produces active congestion of the liver; this is sometimes spoken of as "a chill on the liver." But all cases described in these words are not thus explained; the effects of excessive eating and drinking, dyspepsia, gastro-intestinal catarrh, and constipation are sometimes described in these euphemistic terms. Exposure to high temperature in the tropics is, especially if followed by an accidental chill, a cause of acute congestion of the liver. Direct nervous stimulation has been suggested to explain active congestion of the liver in diabetes, but, as Hunter * points out, the voracious appetite of diabetic patients probably accounts for any active hepatic congestion. Experimentally, however, irritation of the diabetic centre, as by Bernard's puncture experiment, gives rise to intense hyperæmia of the liver.

(II) The more reasonable and by far the commonest cause of active hepatic congestion is to be found in toxic bodies reaching the organ through the blood-stream. This may occur (*a*) through the hepatic artery, as in fevers, especially malaria, and various septic conditions, though in the latter the process may pass on into inflammation or suppuration. It probably occurs in the early stages of icterus gravis, and no doubt is partly responsible for the enlargement of the liver seen in that disease and in the early stage of acute yellow atrophy.

Experimentally it has been shown that subcutaneous or intravenous injection of the extract obtained from muscular tissue gave rise to intense congestion of the liver in animals. (Richet.†)

* Hunter: Allbutt's System, vol. iv, p. 46.

† C. Richet: Acad. des Sciences, Dec. 31, 1900. Le progrès Médical, 1901, p. 23.

(*b*) But generally the poison is derived from the gastro-intestinal tract and reaches the liver by the portal vein. It therefore follows overeating, and especially alcoholic excess, gout, gastritis, indigestion, dysentery. Physiologically active congestion of the liver occurs in digestion and is heightened by spices, pepper, mustard, and curries; in great excess such condiments may no doubt in a suitable subject set up acute and active hepatic congestion. Alcohol is an important factor, especially in hot climates, in producing acute congestion. Other toxines may be carried by the portal vein, as in constipation, or, to take a more extreme case, in phosphorus poisoning. The suppression of menstruation or of habitual hæmorrhages from piles, and the climacteric have been thought to give rise to active hyperæmia of the liver, but the evidence is somewhat slender.

MORBID ANATOMY.

The liver is enlarged, dark in colour, the uniform congestion contrasting with the partial engorgement seen in the chronic venous stagnation of mitral disease. The liver cells show cloudy swelling, and may be fatty and pigmented, while the capillaries are dilated and full of red blood-corpuscles. The small bile-ducts may show proliferation of their living epithelium (cholangitis), which accounts for jaundice when present.

CLINICAL PICTURE.

The symptoms vary. Sometimes the patient is so ill that he must remain in bed; in other cases exercise can quite well be taken. There is malaise, with headache, giddiness, mental depression, irritability, insomnia, and gastro-intestinal symptoms, such as loss of appetite, a foul tongue, a bad taste in the mouth, sometimes nausea, flatulence, and constipation. There is a feeling of discomfort and weight in the hepatic region, while there is pain in the right shoulder. The conjunctivæ become muddy and slightly icteric, the face is often congested, and the skin shares in these changes and may be irritable. The bowels are irregular; there may be bilious diarrhœa or constipation. Epistaxis sometimes occurs.

The symptoms of acute congestion of the liver are much the same as some of those described by Murchison as lithæmia and regarded by him as due to functional inadequacy of the liver. The liver is usually enlarged and may project two or three fingers' breadths below the costal arch in the nipple line. It is decidedly tender on palpation. As a result of repeated attacks of hepatic congestion piles may be produced. Some writers describe œdema of the feet in acute hepatic congestion.

The urine is high coloured, lithatic, concentrated, and of high specific gravity. The amount of urobilin is increased. The amount of ammonia in the urine is little, if at all, above the normal, and thus contrasts with the increase of ammonia found in the urine of patients with cirrhosis (Bain*). If there is jaundice, bile-pigment will be found in the urine.

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* Brit. Med. Journ., 1898, vol. ii, p. 941.

Albuminuria only occasionally occurs; it is transitory and can be explained as the result of poisons passing from the bowel and failing to be stopped by the liver; the kidneys are thus affected, and toxic albuminuria results.

The term *tropical liver* describes the condition found in persons who have had many attacks of acute congestion in hot climates. According to Cantlie, there is usually a history of malaria, diarrhœa, dysentery, or long-standing indigestion. Anæmia, weakness, nervous irritability, and irregularity of the bowels are essential features. The spleen is generally enlarged in addition to the liver. Probably some of these cases are in the early or pre-ascitic stage of cirrhosis.

Duration.—Acute congestion when treated usually lasts about a week, but may, if neglected, become chronic, and may then be a preliminary stage to cirrhosis.

TREATMENT.

In marked cases the patient should be confined to bed and kept on a milk diet. If, as sometimes happens, ordinary milk cannot be borne, skimmed milk, junket, milk jelly, or whey should be tried, and if necessary chicken broth or raw meat-juice should be given. Plenty of water should be allowed, but alcohol must be strictly prohibited. Intestinal antiseptics, such as fractional doses of calomel, perchloride of mercury, or salol, should be given and the bowels kept freely open by calomel and salines, such as Carlsbad or Epsom salts and mineral waters. By free purgation the congestion is greatly relieved, as shown by diminution in the size and disappearance of tenderness of the liver. Medicinally chloride of ammonium in xx-grain doses has been credited with the power of reducing the congestion and preventing inflammation and suppuration. At the outset, if there are symptoms of gastritis a soothing mixture containing bismuth and bicarbonate of soda should be given.

Local Application.—For the pain in the hepatic region a large linseed poultice may be applied, and if it gives relief, be changed every three hours. Cold compresses or dry cupping may be employed if poultices fail. If there is pain on respiration, resembling that of pleurisy and due to perihepatitis, the side should be strapped as for fractured ribs. Leeches applied over the hepatic region or at the margin of the anus have been employed to deplete the congested liver. Pain is undoubtedly relieved by leeching the skin over the liver, although it is hardly probable that much blood is withdrawn from the liver through dilated venous anastomoses between the veins of the abdominal wall and the parumbilical veins in the falciform ligament. Neither is it likely that leeches applied to the anus draw off much blood from the portal vein. Venesection from the veins of the elbow was formerly much in vogue in hepatic congestion, but has almost completely gone out for many years. Direct aspiration of the liver and abstraction of blood is highly spoken of by many. In performing this risky operation the puncture of the liver may have to be performed several times before a vessel of sufficient size to bleed freely is struck.

This withdrawal of blood from the liver is by no means a harmless proceeding. If a large branch of the portal vein or the inferior vena cava is wounded, fatal hæmorrhage may take place into the peritoneal cavity. Indian surgeons, such as Hatch* and Maitland,† who have had fatal experience of aspirating the liver, naturally condemn the procedure. Cantlie,‡ by limiting the length of the aspirating needle to 3½ inches or so, considers that the danger of wounding the inferior vena cava is obviated.

When the more acute symptoms have passed off, the patient's diet should be improved, and tonics, such as strychnine in an acid mixture, should be given. When convalescent, the patient will be benefitted by change of air. A cool, somewhat high, inland resort is usually most suitable. The seaside, especially when the patient lives near the shore, is often harmful and gives rise to constipation and so to a return of hepatic congestion.

In the slighter forms of active congestion of the liver due to over-eating, drinking, and aggravated by constipation and a sedentary life, free purgation with blue pill and haustus sennæ, followed by a simple diet and exercise, should be enjoined. Exercise on horseback or on a bicycle will in many cases act like a charm.

Treatment at a spa, such as Vichy, Ems, Neuenahr, Carlsbad, Marienbad, Harrogate, Leamington, Llandrindod, has a beneficial effect both by reducing congestion of the liver through purgation and by preventing indiscretions in diet, while the freedom from business worries has a good influence on the mental condition.

PROPHYLAXIS.

In gouty patients care as to diet should be taken to prevent undue hepatic congestion; but it is chiefly in persons who are, or have lived, in the tropics and have suffered from malaria that active congestion of the liver is likely to occur, and in whom, therefore, special care should be taken to avoid causes, such as chills, and alcoholic or dietetic excess, etc., which bring on this condition.

Exposure to east wind, cold draughts, and the risk of chills should be avoided by a malarial patient. The parts of the body exposure of which to cold is most liable to give rise to hepatic congestion are the abdomen, the back of the neck, and the legs and feet (Brunton). These parts should be suitably protected; a good plan is to wear a knitted cholera belt over the abdomen, which should always be changed after free action of the skin. Alcohol is best avoided, and if taken at all should be in small quantities well diluted at meal times. Made dishes, much meat, pastry, and sauces should be avoided.

Constipation should be guarded against by diet, viz., fruit and vegetables, porridge, and a sufficiency of water. If necessary, small doses of calomel or blue pill followed by a saline should be given. Active exercise, not merely walking, but riding, climbing, and other forms of exertion, such as rowing, skipping, which lead to compression of the liver between the diaphragm and the abdominal wall, a kind of natural massage, should be taken by persons whose strength and physique are suitable.

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* Hatch, W. K.: Indian Med. Gaz., April, 1898.
† Maitland: Brit. Med. Journ., 1902, vol. i, p. 458.
‡ Cantlie, J.: Brit. Med. Journ., 1903, vol. ii, p. 656.

ACUTE HEPATITIS.

There are a large number of different conditions in which the liver is acutely inflamed. At the outset a division into suppurative and non-suppurative hepatitis may conveniently be made. The suppurative forms of hepatitis are described elsewhere under other headings, such as abscess, pylephlebitis, cholangitis. Acute non-suppurative hepatitis may chiefly attack the liver cells, as in icterus gravis and in acute yellow atrophy, or the brunt of the change may fall on the connective-tissue framework, as in the hepatitis seen after scarlet fever (Klein*). (*Vide* also p. 192.) In malaria the liver cells are affected, but not in the same degree as in icterus gravis. The focal necroses seen in typhoid fever, puerperal eclampsia, and in some other infections and intoxications are allied to acute parenchymatous hepatitis, and represent a patchy or localized distribution of the process, which when diffuse gives rise to acute yellow atrophy.

Acute active congestion of the liver and non-suppurative hepatitis are often two stages of the same process, and any attempt to distinguish sharply between them clinically is difficult or impossible.

MORBID ANATOMY.

So many different forms of pathological change are included under the title of "acute hepatitis" that no one description can possibly be inclusive. The appearance of the liver will vary according to the nature and intensity of the inflammation. In the more acute changes affecting the cells of the liver the condition will resemble that seen in icterus gravis or in acute yellow atrophy, while in less severe types of inflammation the aspect of the liver will resemble that in active congestion. (*Vide* p. 110.) In acute hepatitis as seen in pyæmia the lobules of the liver may be very sharply marked out as bile-stained areas surrounded by greyish white rings.

In a case of hepatitis in a patient who had had a prolonged attack of dysentery the liver was deeply congested, œdematous, and almost fluctuating when it was seen during an operation undertaken by Bérard † under the idea that there was an abscess. The liver was explored in four places; blood alone came out and the patient rapidly recovered.

The liver of severe malarial infection, which is a definite form of acute inflammation, is usually swollen, enlarged, and more or less pigmented, from a brownish to a slaty black tint. The outline of the lobules is indistinct. In more chronic malarial infection two forms of hepatitis, described by Kelsch and Kiener,‡ should be mentioned here: (I) Hyperémie phlegmasique, in which the enlarged and soft liver shows perihepatitis, cloudy swelling, and karyokinesis of the liver cells with small-cell infiltration of the portal spaces. (II) Nodular parenchymatous hepatitis, in which there is hyperplasia of the liver cells forming small nodules on the surface of the organ, which may resemble multiple adenomata or even masses of secondary new-growth, though they are not umbilicated.

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* Klein: Trans. Path. Soc., vol. xxviii, p. 439.

† Bérard: Lyon Médical, May 18, 1902.

‡ Kelsch and Kiener: Archiv. de Physiol. norm. et path., 1878, p. 571; 1879, p. 354.

Attention may also be drawn to a rare form of acute parenchymatous hepatitis which is practically a subacute form of acute yellow atrophy, and shows in a marked degree compensatory hyperplasia of the liver cells. The condition is very closely allied to the nodular parenchymatous hepatitis just described, but is not confined to malarial infection, and is, as has already been hinted, much the same as those cases of acute yellow atrophy in which recovery, or rather partial recovery, with much hyperplasia of the liver cells, occurs.

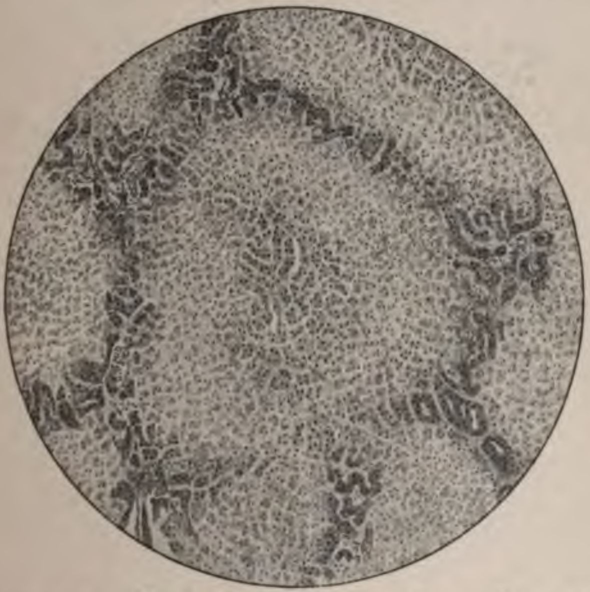

FIG. 18.—DRAWING FROM A MICROSCOPIC SECTION FROM A CASE OF PYÆMIA DUE TO ACUTE NECROSIS OF BOTH FIBULÆ.

Shows cloudy swelling of the liver cells in the intermediate zone of the liver, and small-cell infiltration at the margin of the lobule.

I described a case of this kind in 1891,* but the morbid growths committee of the Pathological Society did not take my view, and regarded the condition as allied to cirrhosis. Professor S. Delépine has most kindly communicated to me full details of a case showing acute interstitial and parenchymatous inflammation with imperfect regeneration of the liver cells, forming tubules containing plugs of bile, and giving rise to hyperplastic nodules. The patient, aged eleven years, was under Sir T. Lauder Brunton's care in 1887 for jaundice after one of the acute specific fevers; from this recovery occurred, but six months later the jaundice recurred and proved fatal. The liver weighed 44 ounces and showed yellow areas of nodular hyperplasia in which the cells had undergone fatty degeneration and so led to the fatal result.

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* Trans. Path. Soc., vol. xliii, p. 81.

The histological appearances in acute hepatitis are those already described in acute congestion of the liver, viz., dilatation of the capillaries, cloudy swelling, fatty degeneration and pigmentation of the liver cells, and catarrhal inflammation of the small bile-ducts. In addition the liver

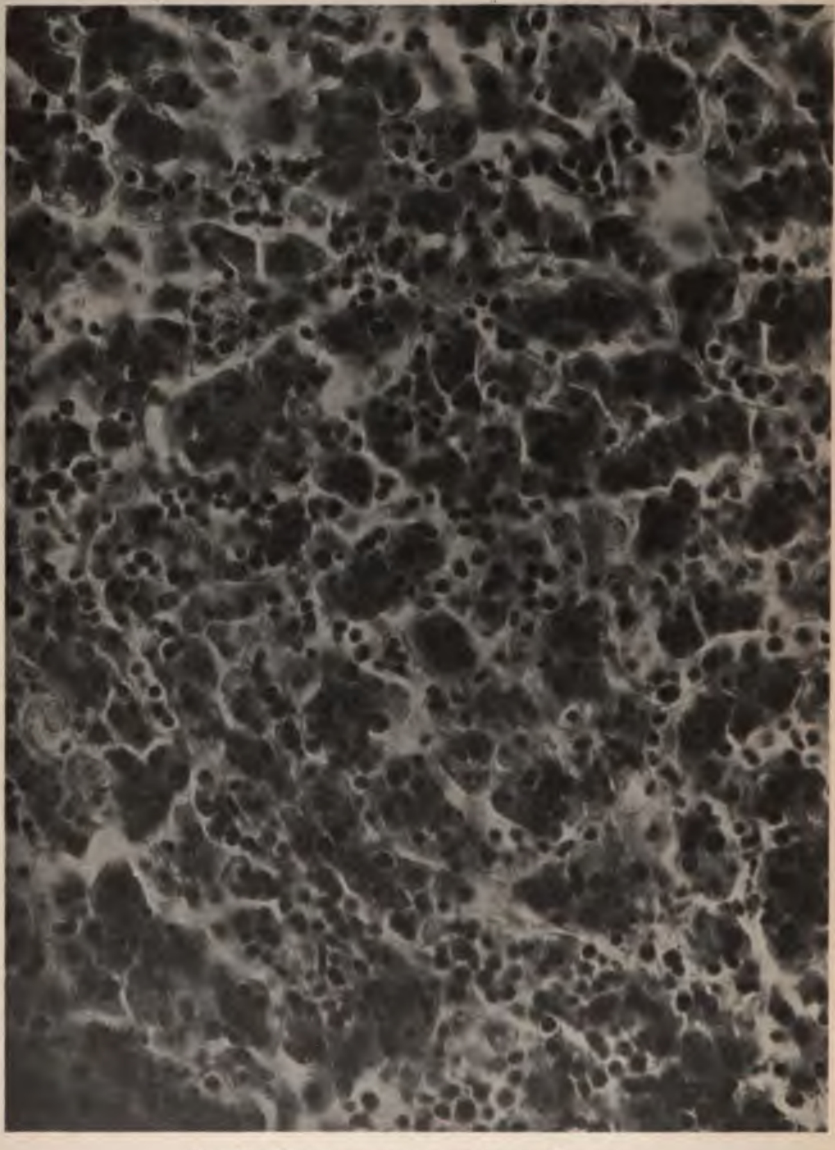

FIG. 19.—PHOTOMICROGRAPH OF ACUTE HEPATITIS.

The liver cells are separated from each other by small round-celled infiltration. From a section prepared by Dr. Bolam. (Photomicrograph by Dr. H. Spitta.)

cells may show focal necroses, with thrombosis of small vessels, and in some instances a varying degree of small-cell infiltration. The small cells are partly polymorphonuclear and other leucocytes, and partly young connective-tissue cells, and are found in the areas of focal necrosis and at the periphery of the lobules.

In some cases there is a diffuse small-cell infiltration, which is, like the hepatitis of congenital syphilis, pericellular. A photomicrograph of a case of acute hepatitis accompanied by fever and jaundice and without any suppuration of the liver illustrates this condition. I am indebted to Dr. R. A. Bolam, of Newcastle-upon-Tyne, for this section.

In the liver of severe malaria there are, in addition, many large phagocytes containing the parasites and pigment. As well as leucocytes, the endothelial cells of the vessels and Kupffer's star-like cells act as phagocytes.* The liver cells undergo degeneration and contain pigment, granules of bile and of hæmosiderin. There is but little fatty change in the cells. Dilatation of capillaries may lead to the production of areas resembling cavernous tissue (Ewing†).

SYMPTOMATOLOGY.

Acute non-suppurative hepatitis due to a general hæmic infection may show itself by jaundice. If the constitutional symptoms accompanying the jaundice are severe, the condition is that described under icterus gravis. But if there is a milder grade of clinical manifestations, the jaundice is spoken of as infectious or toxæmic jaundice, or may conform to the type of Weil's disease. When hepatitis due to a general hæmic infection is not accompanied by jaundice, there may be little to attract attention to the liver, though on examination it may be found to be somewhat enlarged and tender. The condition, which is, perhaps rather vaguely, usually spoken of as acute hepatitis, occurs in patients who have suffered from frequent attacks of malaria, from dysentery, or from both diseases. As the result of exposure to cold or of excess in eating or drinking they suffer from the train of symptoms described later on.

Clinically acute hepatitis is seldom seen in England except in persons who have returned from the tropics. It is an acute form of the reaction to irritants which in temperate climates is chronic and eventually gives rise to cirrhosis. The irritant causing hepatitis is in many instances derived from the gastro-intestinal tract. The symptoms are the same as those of active congestion of the liver, to which reference should be made, but are more marked. The temperature in hepatitis is raised, and on the degree of fever a clinical distinction has been drawn between active congestion and hepatitis; when the temperature is above 100° the condition is regarded as inflammatory, and when below this point, active congestion is considered to be present.* The gastro-intestinal symptoms described in acute congestion are accentuated and vomiting is more frequent. The bowels may be constipated, or there may be diarrhœa; in both cases the motions are very offensive. The pain in the shoulder is more marked than in simple congestion, and from extension of hepatitis to the capsule of the liver the case may become complicated by perihepatitis. This makes the descent of the diaphragm painful and leads to shallow respirations. The patient is irritable, low-spirited, and sits up in bed. The abdomen is rigid and the liver is uniformly enlarged and tender. When there is concomitant malaria, the spleen is also enlarged. Toxic albuminuria, which has been spoken of as hepatogenic (Teissier†), is occasionally seen.

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* See valuable papers by Barker: Johns Hopkins Hospital Reports, vol. v, p. 221.

† Ewing: Journal of Experimental Med., 1902, p. 154.

DIAGNOSIS.

When there is distinct jaundice, a diagnosis must be made in the most severe cases from acute yellow atrophy and from phosphorus poisoning. In acute yellow atrophy the rapid course, the presence of nervous symptoms, and the fact that the liver, if at first increased in size, soon diminishes, are characteristic points. In phosphorus poisoning the hæmorrhagic condition of the vomit and stools and the history are points of importance. But in both these conditions the constitutional symptoms are far more severe than in acute hepatitis. When the jaundice is slight, infectious jaundice should be thought of.

In some cases where the liver is very considerably enlarged and the other symptoms severe it may be very difficult or impossible to be sure that there is not suppuration in the liver, especially as acute hepatitis may be the first stage of a tropical abscess. This difficulty not uncommonly occurs in malarial patients.

Bérard's case, already referred to, is an example of the difficulty in making a diagnosis between acute hepatitis and hepatic abscess. Remlinger,‡ Bozzolo,§ and others have described a form of acute hepatitis under the name of the infective liver which clinically imitates hepatic abscess.

The same difficulty may arise in differentiating the condition from more diffuse forms of hepatic suppuration, such as suppurative pylephlebitis and cholangitis. In these cases some time may be required before an accurate differential diagnosis can be made.

TREATMENT.

The treatment is on the same general lines as in simple congestion, but is rather more active. The patient should be kept in bed on a low diet, and the local pain and tenderness over the liver relieved by cold applications, poultices, scarifying the skin, leeching, dry cupping, or by strapping the hepatic region with narrow strips of plaster as if for fractured ribs. Milk or the modifications of it mentioned on page 111 (congestion) is the staple diet, but if it disagrees, raw meat-juice, chicken broth, jelly, or other similar preparations should be substituted. Plenty of water should be given or its equivalent, such as soda water, lemonade. But alcoholic drinks of all kinds should be strictly tabooed.

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* Cantlie: Encycl. Med., vol. vii.

† J. Teissier: Les Albuminuries Curables, p. 34.

‡ Remlinger: La Presse Médicale, 1903, p. 86.

§ Bozzolo: Rev. crit. di Clinica Med. March 15, 1902

The bowels should be kept freely open by salines, such as sulphate of soda or of magnesia, or calomel may be given with advantage. Vomiting and signs of gastritis should be allayed by bismuth, hydrocyanic acid, bicarbonate of soda, etc. Chloride of ammonium in twenty-grain doses should be given three times a day during the acute stage, and may be combined with dilute hydrochloric acid and a few minims of liquor strychninæ. If there is a history or evidence of malaria, quinine should be given as soon as the gastro-intestinal symptoms have subsided.

The abstraction of 10 to 15 ounces of blood from the substance of the liver by means of an aspirator is much advocated and has been thought to prevent the further development of suppuration. It is, however, not entirely without risk, as fatal hæmorrhage into the peritoneal cavity has been known to follow.* (*Vide* remarks on treatment of acute congestion.) When convalescent, the patient should go to a cool, fairly bracing climate, and will get benefit from spa treatment, such as Harrogate, Carlsbad, Marienbad, Neuenahr, Ems, Vichy. The prophylactic treatment is that of acute congestion. (*Vide* p. 112.)

* Hatch: Indian Med. Gaz., April, 1898. Maitland: Brit. Med. Journ., 1902, vol. i, p. 458.

HEPATIC ABSCESS.

Intra-hepatic suppuration may be conveniently divided into two main groups: (I) Where the abscess is large and single, the "tropical" abscess, and (II) multiple abscesses. Strictly speaking, this classification is not entirely satisfactory; for occasionally there may be two large abscesses in the liver, and a single abscess may infect the remainder of the liver and give rise to several secondary abscesses; while, on the other hand, multiple abscesses may unite and eventually form a large areolar abscess. It has, however, a practical advantage, for cases of large single, solitary or tropical abscess are accompanied by more characteristic signs and are in general curable by operation, while multiple abscesses are less easy to diagnose and cannot be benefitted by surgical treatment.

SINGLE OR TROPICAL ABSCESS.

ETIOLOGY.

Dysentery.—There can be no question that the causation of tropical abscess is more closely related to dysentery than to any other condition. Some statistics show a close association between the diseases termed dysentery and the subsequent development of hepatic abscess. Azevedo Sodré,[*] adding together the statistics of Moore, Macpherson, Marshall, Morehead, and Dutrouleau, found that in 1997 autopsies on dysentery there were 407 hepatic abscesses, or 20 per cent. In 314 selected cases of hepatic abscess taken by Kelsch and Kiener,[†] 268, or 75 per cent., had had dysentery. In a later analysis by Kelsch[‡] of 500 cases of hepatic abscess dysentery was present in 85 per cent. On the other hand, E. J. Waring's[§] statistics from India do not show such a close relationship; thus, in 2758 cases of dysentery treated in the Madras Presidency between the years 1826 and 1843 there were 68 cases of abscess, or 2.5 per cent.; while in his 300 fatal cases of abscess, only 82, or 27 per cent., were admitted for dysentery. Buchanan's[‖] figures also show that there is a want of parallelism between the curves of the incidence of dysentery and hepatic abscess in India. Thus, the natives suffer more severely from dysentery and less from hepatic abscess, while the converse holds good among European soldiers.

In 79,723 cases of dysentery among the natives there were 127 cases of hepatic abscess, or 1 in 628; while in the European army during four years (1893–96) there were 7972 cases of dysentery and 441 cases of abscess, or 1 in 18.

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[*] Azevedo Sodré: XXth Century Practice of Medicine, vol. xvi, p. 253.

[†] Kelsch and Kiener: Traité des Maladies des Pays Chauds, Paris, 1889.

[‡] Kelsch: La Sem. Méd., 1900, March 7, p. 80.

[§] E. J. Waring: Abscess in the Liver in the East Indies, 1854, p. 123.

[‖] Buchanan, W. J.: Journ. Trop. Med., vol. i, p. 173, 1899.

The following arguments have also been urged against the too exclusive view of the dysenteric origin of hepatic abscess:

(I) That hepatic abscess is much commoner among English soldiers in India than in other tropical countries, such as Jamaica, where dysentery is as frequent as it is in India.

(II) That an increase in the curve of dysentery—for example, in war-time—is not accompanied or followed by any increase in the liver abscess curve.[*]

In the bacillary dysentery of Japan Shiga has never seen hepatic abscess as a complication, and in the dysentery seen in the South African War, 1899–1902, which was not amœbic, hepatic abscess was very rare.

In 250 cases observed by Washbourn and Richards[†] at the Imperial Yeomanry Hospital, Deelfontein, there was only one hepatic abscess; out of 466 cases of dysentery treated at the Imperial Yeomanry Hospital, Pretoria, there were two fatal cases of pylephlebitis, and another case, in which after an operation for piles performed some six months after an attack of dysentery, a single hepatic abscess developed and was successfully operated upon. While in South Africa (1901) I made enquiry from medical officers, who all agreed that single hepatic abscess as a sequela of South African dysentery was extremely rare.

Dysentery in temperate climates occurs sporadically as "ulcerative colitis" and in epidemics in asylums. Asylum dysentery has been specially studied in this country by Mott and Durham,[‡] and in America by Vedder and Duval.[§] The latter observers have shown that asylum or institution dysentery, which was formerly called ulcerative colitis, is due to a bacillus identical with that described by Shiga and Flexner as the cause of acute epidemic dysentery. Liver abscess is very rare after asylum dysentery. In Gemmel's[‖] 80 cases examined after death at the Lancaster Asylum there were two cases; while in the epidemics of dysentery at Milbank, 1840–47, W. Baly[**] did not find any case of abscess. The rarity of hepatic abscess in asylum dysentery is quite in accord with the fact that abscess hardly ever occurs in bacillary dysentery in the tropics.

(III) That in some cases of hepatic abscess there is no history of dysentery, and that after death the colon may appear quite healthy.

In 456 cases of fatal hepatic abscess recorded in the annual reports of the sanitary commissioner of India during the five years 1896 to 1900 the intestines were free from ulceration in 47 per cent.

Even amœbic abscess of the liver, which according to Lafleur[††] must for the present be considered as invariably secondary to active or latent amœbic dysentery, has been found to occur in cases where the colon was normal at the autopsy.[‡‡] It is possible that in such cases the amœbæ have gained entrance to the portal system by some minute lesion which subsequently healed over.

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[*] Editorial, Indian Med. Gaz., May, 1902, p. 193.

[†] Washbourn and Richards: Brit. Med. Journal, 1900, vol. ii, p. 668.

[‡] Mott: Trans. Epidemiolog. Soc., 1902.

[§] Vedder and Duval: The Journ. of Experimental Medicine, vol. vi, p. 181.

[‖] Gemmel: Idiopathic Ulcerative Colitis, p. 29, 1898.

[**] Baly, W.: Med. Gaz., vol. iv, p. 885.

[††] Lafleur: Allbutt's System of Medicine, vol. iv, p. 155.

[‡‡] Burton, J. T.: Proc. Philadelphia Path. Soc., Jan., 1899. Flexner, S.: American Journal of Medical Sciences, May, 1897. Thompson: Manchester Medical Students' Gaz., 1903, p. 146. Futcher: Jour. American Med. Assoc., vol. xli, p. 480, Aug. 22, 1903.

The fact that there may be no history of dysentery in cases of hepatic abscess may in some cases be explained by its having remained latent. In cases where evidence of past dysentery is found at the autopsy, and where no history has been forthcoming, the original attack may have been forgotten, since an abscess may occur years, even ten,[*] after dysentery, or may be remembered and spoken of as diarrhœa.

In five out of twenty-seven cases of amœbic abscess, intestinal symptoms of dysentery were not noticed by the patients. (Futcher.[†])

(IV) It has been thought that the dysenteric ulceration of the colon is secondary to the abscess. The older observers believed that pus passed down the bile-ducts into the intestine and set up diarrhœa and ulceration. This explanation is no longer accepted. But that septic absorption from the abscess may set up diarrhœa and intestinal ulceration is shown by some cases of fatal hepatic abscess where a recurrence of dysentery or recent ulceration is seen in a colon showing evidences of old dysentery. Flexner,[‡] indeed, considers that even in amœbic dysentery the intestinal lesions may be secondary to the amœbic hepatic abscess.

(V) Another view which has been put forward is that the two diseases are both independent results of the same infection. Some evidence in favour of this has been brought forward. Thus, it has been urged that when dysentery breaks out patients may develop hepatic abscess who have not shown any signs of dysentery, while those who contract dysentery do not necessarily become the subjects of hepatic abscess.

The, at first sight, puzzling difference which is shown in various parts of the world between the relation of the disease called dysentery and the subsequent development of a single hepatic abscess, may be explained in the following way: Under the heading dysentery at least two distinct forms of colitis have been included in the past; (*a*) amœbic dysentery of a chronic type, which is followed by the single or tropical hepatic abscess, and (*b*) acute bacillary dysentery, which is not followed by single hepatic abscess. Bacillary dysentery was described in Japan by Shiga,[§] where it was extremely severe, by Flexner[‖] in Manila, and, as already mentioned, by Duval and Vedder[**] in America, and by Kruse[††] in Germany. Amœbic and bacillary dysentery may occur side by side. The two diseases were studied and could be distinguished from each other in Manila during the Spanish-American war.

Tropical dysentery is more often followed by abscess than the dysentery seen in temperate countries; this was correlated by Councilman and Lafleur with the amœbic nature of the tropical form.

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[*] Josserand: Journ. de Méd., July 25, 1898.

[†] Futcher, T. B.: Jour. American Med. Assoc., vol. xli, p. 480, Aug. 22, 1903.

[‡] Flexner: American Journal of Medical Sciences, vol. cxiii, p. 553, May, 1897.

[§] Shiga: Centralblatt f. Bakteriol. u. Parasit., Bd. xxiii, S. 549; Bd. xxiv, S. 817, 870, 913.

[‖] Flexner: Johns Hopkins Hospital Bull., Feb., 1900. Brit. Med. Journ., 1900, vol. ii, p. 20. Univ. Pennsylv. Med. Bull., Aug., 1901.

[**] Vedder and Duval: Journ. Experimental Medicine, vol. vi, p. 181.

[††] Kruse: Deutsche med. Wochen., 1900, S. 637.

In 2590 cases of tropical dysentery hepatic abscess occurred in 507. (Councilman and Lafleur.*)

According to Lafleur, amœbic abscess of the liver is secondary to and a complication of amœbic dysentery, while non-amœbic hepatic abscesses are usually independent of any intestinal affection.

Very few statistics are available to show the incidence of hepatic abscess in amœbic dysentery. In 119 cases of amœbic dysentery treated in the Johns Hopkins Hospital 27, or 22.6 per cent., had hepatic abscess (Futcher†); while in Strong's 79 autopsies on cases of amœbic dysentery 14 had liver abscess.

Other Causes of Single or Tropical Abscess.—Apart from dysentery the factors which can be regarded as having a causal relationship to hepatic abscess are comparatively insignificant.

Traumatism may give rise to hepatic abscess either (I) directly,—for example, when a penetrating wound introduces micro-organisms into the liver substance,—or (II), indirectly, by so reducing the resistance of the liver that any pus-producing micro-organisms which happen to reach the liver either from the general circulation by means of the hepatic artery, or from the alimentary canal are then enabled to grow and multiply. Thus a blow on the liver may produce a small rupture inside the liver without damaging the capsule; recovery should then occur, but if micro-organisms have previously gained access to the damaged part of the liver, an abscess may follow.

(I) Penetrating wounds with a dagger, knife, or bullet may carry with them infecting micro-organisms, or infection may occur later. A bullet may carry some of the patient's clothing into the wound with it, and thus micro-organisms may be introduced at the time of the wound. Infection may also supervene either from the wound or possibly from the blood-stream.

It appears probable that a foreign body may remain encysted in the liver for a considerable time and that suppuration may eventually supervene around it. In such cases it is probable that this part of the liver having its resistance diminished, thus becomes infected more easily by the blood-stream. It is hardly likely that micro-organisms introduced at the same time as the foreign body—a bullet, for example—have remained latent. In rare instances, a pin, needle, or fish-bone may penetrate the alimentary canal and enter the liver substance, thus giving rise to hepatic abscess.

(II) Traumatism without any penetrating wound may be followed by hepatic abscess. This is not a common event. F. C. Turner ‡ in 1882 was only able to refer to 12 cases, but this estimate must not be taken as actually representing its incidence. On the other hand, the relation between traumatism and abscess may be merely that after traumatism a latent abscess increases in size or by leakage sets up a perihepatic or subphrenic abscess.

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* Councilman and Lafleur: Amœbic Dysentery, Johns Hopkins Hospital Reports, 1890–91.

† Futcher: Jour. American Med. Assoc., vol. xli, p. 480.

‡ Turner, F. C.: Trans. Path. Soc., vol. xxxiii, p. 177.

Extension of Inflammation from Adjacent Parts.—This method of formation of a single hepatic abscess is very rare, and not of much importance. In a few instances calculi in the gall-bladder may, by giving rise to ulcerative cholecystitis and perforation, set up suppuration in the adherent liver substance.

Weir[*] records a case of suppurative cholecystitis in a woman aged thirty-five with perforation of the wall of the gall-bladder leading into a small abscess cavity containing rather more than an ounce of pus.

Perforation of a simple or of a malignant gastric ulcer into the liver may set up suppuration in a comparatively limited area. In these cases the abscess cavity may show necrotic changes which, according to Gilbert and Lippmann,[†] depend chiefly on anaërobic micro-organisms.

I have twice seen malignant disease of the cardiac end of the stomach grow directly into the substance of the left lobe of the liver and give rise to a suppurating cavity in its substance. In one of these cases death was caused by peritonitis due to leaking from the abscess.

An empyema or an abscess in the base of the right lung, suppuration in or around the right kidney, or a localized subphrenic abscess have also been described as extending into and giving rise to suppuration inside the liver. But in these cases it is not always certain whether the suppuration began in the organ named and extended into the liver, or whether it originated in the liver.

Typhoid Fever.—Hepatic suppuration is rare in typhoid fever. The gall-bladder is more often affected than the liver itself. In very rare instances a solitary hepatic abscess follows typhoid fever. It is said to be less rare in the tropics than in temperate countries (Bertrand and Fontan [§]), and possibly this is due to the influence of dysentery or to the diminished resistance of the liver induced by dysentery, malaria, alcoholism, etc. When a solitary abscess follows typhoid fever, it may be due to infection from some secondary abscess, such as suppuration of the parotid, and is rarely a direct result of typhoid fever.

In 2000 fatal cases of typhoid fever examined at Munich Hölscher[§] found twelve cases of solitary hepatic abscess: his figures probably include Dopfer's[‖] 927 autopsies on typhoid fever with ten solitary abscesses of the liver (Osler[**]). W. W. Keen[††] has collected sixteen additional cases, in some of which there were secondary abscesses elsewhere in the body; in Louis' case—one of the earliest on record—and in Osler's[‡‡] there was parotitis, and in Chvostek's perichondritis of the larynx.

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[*] Weir: Medical Record, 1900, p. 1137.

[†] Gilbert and Lippmann: Soc. méd. des Hôp. Paris, July 17, 1903.

[‡] Bertrand et Fontan: L'Hepatite Suppurée, Paris, 1895.

[§] Hölscher: München. med. Wochenschrift, 1891, No. 4, 5.

[‖] Dopfer: München. med. Wochenschrift, 1888.

[**] Osler: Edinburgh Med. Journal, 1897, vol. ii, p. 427.

[††] Keen, W. W.: Surgical Complications and Sequels of Typhoid Fever, 1898, p. 246.

[‡‡] Osler: Studies in Typhoid Fever, Johns Hopkins Hospital, p. 380.

That the typhoid bacilli can give rise to a solitary hepatic abscess is supported by bacteriological examination, but, as a rule, there is a mixed infection.

In two cases of solitary abscess following typhoid fever bacteriological examination showed a pure culture of typhoid bacilli in one, while in the other typhoid bacilli and staphylococci were present. (Cassuto.[*])

I have seen one case where a single hepatic abscess followed enteric fever.

An Imperial Yeomanry trooper aged thirty years, who had never had dysentery or been previously out of England, was inoculated against enteric fever in 1900 when on his way to South Africa. He had two attacks of enteric fever in the course of the next twelve months in Africa; when convalescent from the second attack he had an attack of acute pneumonia on the right side, followed by signs suggesting empyema. The chest was aspirated and 12 ounces of sanious pus containing liver cells, but perfectly sterile, was evacuated. The trocar seemed to go through a tough membrane. The next day Mr. D. Drew excised part of the sixth rib and freely opened an abscess in the anterior part of the right lobe of the liver. The patient recovered, was invalided home, and was seen in December, 1901, in perfect health.

Suppurating Hydatid Cyst, etc.—When a hydatid cyst suppurates the conditions are for all practical purposes the same as a single hepatic abscess. In rare instances a round-worm in the intra-hepatic bile-ducts may give rise to a single small abscess, but, as a rule, there is suppurative cholangitis with multiple suppurating foci.

Single Pyæmic Abscess.—A single hepatic abscess is sometimes due to causes, such as general hæmic infection, or infection of the portal system, which, as a rule, give rise to multiple abscesses. In exceptional instances suppuration or infection elsewhere in the body is the only cause to account for a single hepatic abscess. Thus it has followed cutaneous abscesses, whitlow, suppuration of the parotid, bronchiectasis (Muir[†]), parametritis and pyosalpinx (Roughton[‡]), prostatic abscess (Lancereaux[§]), scarlet fever,[‖] and influenza (Cimbali[**]).

A single hepatic abscess may also occur as the result of emboli derived from the portal vein or its tributaries. Thus in exceptional instances it may follow gastric ulcer,[††] appendicitis, ulcers in the colon, or ligature of piles. But it must be borne in mind that in hepatic suppuration secondary to infection from the alimentary canal there are usually multiple areas of suppuration and not a solitary abscess. This is true with the exception of the single or tropical abscess following amœbic dysentery.

A single loculated or areolar abscess may be the late stage of a number of neighbouring areas of multiple diffuse suppuration, due to pylephlebitis or suppurative cholangitis affecting a comparatively large intra-hepatic branch of the portal vein or bile-duct. This consideration renders it easy to see how a single hepatic abscess may occur as the result of portal infections which are usually productive of multiple hepatic abscesses.

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[*] Cassuto: Thèse de Paris, 1900.

[†] Muir: Edinburgh Hospital Reports, vol. ii, p. 100.

[‡] Roughton: St. Bartholomew's Hosp. Reports, vol. xxi, p. 176.

[§] Lancereaux: Traité des Maladies du Foie et du Pancreas, 1899.

[‖] Guy's Hospital Museum, No. 1294.

[**] Cimbali: Lo Sperimentale, 1890.

[††] Dalton, N.: Kings College Hospital Reports, vol. ii, p. 25.

In appendicitis, a single hepatic abscess is very rare indeed; it sometimes happens that a single abscess is diagnosed and operated upon, but the patient dies, and if no postmortem is possible, the actual condition remains doubtful; when an autopsy is made, multiple abscesses are usually found. The two following cases show the difficulty in forming a positive opinion in some instances:

Among 38 cases of perityphlitic abscess tabulated by Hawkins[*] there was one case of hepatic abscess; it was opened and a half pint of pus let out; the man lived two months longer, and as a postmortem was refused, there may possibly have been multiple abscess.

Stooke[†] reports the case of a marine aged twenty-seven who had attacks of diarrhœa followed by signs of hepatic abscess. Forty ounces of sweet pus were evacuated from the liver abscess, but when the man died nine days after the operation there were multiple abscesses in the right lobe and signs of suppuration around the vermiform appendix. Possibly the multiple abscesses were secondary to the larger abscess.

In the following case appendicitis almost certainly gave rise to a single hepatic abscess:

Morton[‡] recorded a case in which a few days after draining an abscess in connexion with the appendix, an abscess in the liver was opened; the patient recovered.

In the following case a large abscess due to the union of originally separate abscesses was due to infection from the appendix:

A girl aged seven years who, except for a stitch in the right side of the abdomen for more than a year, had never had any signs of appendicitis, came under the care of Dr. G. H. Hames with signs of right-sided pleurisy. Subsequently hepatic abscess was diagnosed and several operations with the evacuation of pus from the liver were performed by Mr. Charters Symonds. At the autopsy, which I performed,[§] the vermiform appendix was surrounded by old adhesions and recent lymph, and was perforated by a pin. The portal vein was healthy. The liver, which was greatly enlarged, contained a loculated area of suppuration as large as one's fist in the upper and back part of the right lobe. It had been partially opened during life and contained gelatinous pus. In the immediate neighbourhood there were spreading foci of suppuration. The rest of the liver was of a bright yellow colour resembling phosphorus poisoning.

DISPOSING FACTORS.

Geographical Distribution.—Large hepatic abscess is a disease of tropical climates, and cases seen in this country are usually in persons who have been in hot climates and suffered from dysentery or even from a previous hepatic abscess there. Although a tropical disease, hepatic abscess is not met with uniformly in different parts of the tropics; thus, while it is frequent in India, Senegal, Ceylon, Mauritius, Algiers, Egypt, Java, Sumatra, Mexico, Peru, Chili, it is much less common in the West Indies, China, Brazil, Guiana.

Climate.—A high mean temperature very decidedly favours the occurrence of hepatic abscess. From the incidence of chills, the commencement of the cold season has been said to be a favourite time for the development of hepatic abscess. But from an analysis of the 236 cases of hepatic abscess in Calcutta Rogers * found that there was no special seasonal prevalence.

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[*] Hawkins, H. P.: Diseases of the Vermiform Appendix, p. 97.
[†] Stooke: Brit. Med. Journ., 1901, vol. i, p. 342.
[‡] Morton, C. A.: Bristol Medico-chirurgical Journ., Dec., 1897.
[§] Rolleston: Trans. Path. Soc., vol. xlix, p. 106.

Acclimatisation.—It would appear that persons who have recently become resident in tropical climates are more likely to suffer from hepatic abscess than those who have been there some time.

In 114 cases E. J. Waring† found that 22 per cent. of cases of abscess occurred in India in soldiers who had been less than one year in the country, 10.5 per cent. in the second year, and 10.5 per cent. in the third year. Brydon's ‡ figures, however, tend to show the reverse, viz., that long residence seems to increase the liability of Europeans to abscess.

Race.—Europeans are much more liable to hepatic abscess in the tropics than the natives.

In 79,723 cases of dysentery among the natives of India collected by W. J. Buchanan§ there were only 127 cases of hepatic abscess, or 1 in 628 cases, while in 7972 cases of dysentery among Europeans in India there were 441 cases of hepatic abscess, or 1 in 18.

But when natives give way to alcohol they are more likely to be attacked by abscess. It is said to be commoner in the rich than in the poorer natives of India.

The greater susceptibility of the European male to hepatic abscess does not depend, at any rate entirely, on the fact that he is not acclimated to tropical climates, for hepatic abscess is very rare in European women and children in the tropics, though they are equally subject to dysentery; further, it does not depend on a special liability to dysentery, for in India the natives are more subject to dysentery and less to hepatic abscess than Europeans. The important factors which account for the greater liability of European males to hepatic abscess will be referred to under the heading of Sex, page 128.

Occurrence in England.—Residence in England is not a disposing factor to hepatic abscess, but it is convenient to refer to the incidence of hepatic abscess in England here. As already mentioned, most of the cases observed in England have come from tropical climates, but in a certain number of instances the patient has never left this country. The number of cases seen in ordinary hospital practice is small, probably not more than two or three a year for each of the large London hospitals.

In sixteen years there were 13 fatal cases of single hepatic abscess at St. George's Hospital; in 3 of these the fatal abscess was a recurrence, the patients having been previously successfully operated upon. Ten of the cases, all men, had been abroad, 8 in India, 1 in China, and 1 in South Africa. In 15 fatal cases at Guy's Hospital in twenty years, 5 had been in China, India, or in the West Coast of Africa, but in 10 there was no such history, and several patients had never been out of England. (Hilton Fagge.‖)

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* Rogers, L.: Brit. Med. Journ., 1902, vol. ii, p. 844.

† Waring, E. J.: Hepatic Abscess, p. 113.

‡ Brydon: Quoted by Davidson, Allbutt's System of Medicine, vol. iv, p. 139.

§ Buchanan, W. J.: Journ. of Tropical Medicine, vol. i, p. 173, 1899.

‖ Hilton Fagge's Text-book, edited by Pye Smith, vol. ii, p. 525, 4th Edit.

Alcoholism.—By depressing the resistance of the liver alcohol disposes to hepatic abscess. Its importance in this respect is shown by the facts that abscess is seldom seen in total abstainers, and that, conversely, natives who drink may suffer from liver abscess while their fellows who are teetotalers escape.

According to Sandwith,* hepatic abscess is met with only in those natives of Egypt who are addicted to alcohol. In 40 cases tabulated by E. J. Waring † only 13, or 32 per cent., were sober and temperate; the remainder, 67 per cent., were intemperate.

Diet.—A stimulating and excessive diet, by giving rise to considerable physiological congestion, which under the influence of the tropical climate and a sedentary life may become pathological, prepares the way for hepatitis and so for abscess. As a disposing factor errors of diet are probably very greatly inferior to alcoholic excess.

Malaria.—By diminishing the resistance of the liver and producing a certain amount of hepatitis, malaria disposes to hepatic abscess and in a minor degree plays much the same kind of rôle as alcoholism. Hepatic abscess, however, occurs in places where malaria is unknown, as in the Seychelles group and the island of Rodrigues. (Davidson.‡) Malaria and dysentery occur so frequently in the same districts that malaria is often an antecedent condition of hepatic abscess. It is not, however, a true cause of hepatic suppuration.

Yellow fever may precede the development of an hepatic abscess, but this is probably merely accidental, and there is no reason to think that there is any direct relation between them; though no doubt after yellow fever the resistance of the liver is weakened and the organ more liable to infection.

Sex.—Single tropical abscess is much commoner in males than in females. This applies to adults, for in children—who are, however, rarely the subjects of a single hepatic abscess—the incidence is about equal in the two sexes.

In E. J. Waring's 300 Indian cases 291 were males and 9 females. In 13 fatal cases at St. George's Hospital 11 were males; in one of the females the abscess was probably connected with cholelithiasis.

The greater predominance of the male sex is due to a number of factors. First, the larger number of male Europeans resident in tropical climates must be taken into account, for Europeans are much more subject to abscess than natives. But even after allowing for this, males are more subject to abscess than women; for though it appears that dysentery affects European men and women equally, abscess seldom occurs in women. (Manson.§) The factors which have been thought to increase the tendency of European males to abscess are: (i) Alcoholism, which disposes to hepatitis and favours infection by reducing the resistancé of the organ; (ii) greater tendency to exposure to chills, and (iii) greater liability to blows in the hepatic region.

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* Sandwith: Quoted by Davidson, Allbutt's System, vol. iv, p. 136.

† Waring, E. J.: Hepatic Abscess, p. 114.

‡ Davidson: Allbutt's System, vol. iv, p. 137.

§ Manson, P.: Tropical Diseases, p. 442.

Age.—Hepatic abscess is a disease of adult life and is rare in children and in old persons.

In 227 fatal cases tabulated by Waring,[*] 112, or 48.4 per cent., were between the ages of twenty and thirty. It must be remembered, however, that the cases were from the Indian army, which contained a very large number of men about this age. The oldest case met with by Waring was a pensioner aged seventy-two years, and the youngest in a girl aged fifteen years.

In young children large hepatic abscesses are rare, and when they do occur, are more often due to worms in the bile-ducts, to traumatism, or to appendicitis. Cases of typical tropical abscess do, however, occur in early life.

Amberg[†] tabulates 12 cases in children due to dysentery; in only one (Slaughter's[‡]) were motile amœbæ found in the pus, though dead amœbæ were seen in the pus of Gneftos'[§] case. Amœbic abscess is therefore very rare in children.

Moncorvo[‖] records the case of a child aged two years who recovered after 500 grammes of pus had been removed from the abscess. Arnott[**] described a fatal case in a child aged two and a half years, but apparently no autopsy was performed. Finizio[††] reports a fatal case of hepatic abscess subsequent to dysentery in a boy aged six years. In a boy aged nine years the abdomen was so distended that the condition was thought to be ascites. (Hatch.[‡‡])

MORBID ANATOMY.

Situation.—Between 60 and 80 per cent. of large single abscesses are in the right lobe of the liver. Occasionally a large abscess may occupy parts of both the right and left lobes.

Of E. J. Waring's cases, 67 per cent. were in the right lobe; 6.6 per cent. in the left lobe; and 14.5 per cent. in both the right and the left lobe. In Rouis'[§§] series 78.6 per cent. were in the right lobe, 16.8 per cent. in the left, and 4.6 per cent. in the Spigelian lobe.

From injection with methylene-blue, Sérégè[‖‖] comes to the conclusion that the blood from the stomach and spleen is carried into the left lobe, while that from the pancreas and intestines passes into the right lobe. This theory serves in part to explain the greater frequency of abscess in the right lobe. In addition, the right lobe is so much the bigger of the two that it naturally receives the larger share of blood. Rogers[***] suggests that the frequency with which the ascending colon and hepatic flexure are involved in amœbic dysentery, thus allowing amœbæ to pass across the peritoneum to the surface of the liver, may also account for the preponderance of abscess in the right lobe.

The abscess is often situated deeply in the right lobe towards its posterior and upper border. When in this situation it may work its way forward and present anteriorly, but more often it projects upwards under the diaphragm. In the latter case the existence of an abscess is often very difficult to determine with certainty by percussion, as it may carry the diaphragm upwards, and if the lung is adherent to the chest wall there will be comparatively little dulness. In such cases skiagraphy is of great service, by showing the position and amount of movement of the right leaflet of the diaphragm. The under surface of the right lobe of the liver close to the hepatic flexure of the colon is another favourite site of abscess. According to Lafleur * and Rogers, it is probable that amœbæ may pass through the walls of the colon and infect the surface of the liver at this point.

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[*] Waring, E. J.: Abscess in the Liver, p. 112.

[†] Amberg: Johns Hopkins Hospital Bull., Dec., 1901.

[‡] Slaughter: Virginia Med. Monthly, Oct., 1895.

[§] Gneftos: Deutsche med. Wochen., 1891, S. 853.

[‖] Moncorvo: Rev. Mensuelle des Malad. de l'enfance, Dec., 1899.

[**] Arnott: Brit. Med. Journ., 1903, vol. i, p. 189.

[††] Finizio: La Pediatria, 1896, p. 310.

[‡‡] Hatch: Indian Med. Gaz., Aug., 1898.

[§§] Rouis: Recherches sur les suppurations endemeques, 1860, Paris.

[‖‖] Sérégè: Soc. Méd. des Hôp., April 26, 1901. Journ. de Méd. de Bordeaux, May 25, June 1 and 8, 1902.

[***] Rogers, L.: Brit. Med. Journ., 1902, vol. ii, p. 850.

When an abscess is near the surface of the liver and close to the suspensory ligament, it may rupture into the space between the two layers of that peritoneal ligament and form an abscess between the liver and diaphragm. This has been spoken of as a supra-hepatic abscess by Cantlie,† who, however, considers that this form of abscess begins in the lymphatics in the ligaments and not in the liver.

Number.—A large abscess may be the only focus of suppuration in the liver or it may be associated with one or more abscesses, usually smaller.

In E. J. Waring's 300 fatal cases 177, or 59 per cent., were solitary abscesses, and in 33, or 11 per cent., there were two abscesses. Davidson‡ gives 75 per cent. as solitary, thus agreeing with Rouis, 11 per cent. with two abscesses, and 14 per cent. with more than two. In 13 fatal cases at St. George's Hospital there was a single abscess in ten.

The smaller abscesses may be secondary and due to infection from the originally single abscess, or they may belong to a series of small abscesses which have united to form an areolar abscess. Two or even three large abscesses may be independent in origin. Godlee § believes that many of the cases of a second abscess following a previous one are due to the drainage-tube having been removed too soon, or to some diverticulum of the original abscess having been imperfectly explored and drained.

The shape of an abscess shows considerable variation; usually it is round, but it may be oval or irregular, and when due to the union of previously separate abscesses, may be branching or areolar.

The size of a single abscess varies very greatly. Not uncommonly it contains three-quarters of a pint of pus, but as much as 16 or even 19 pints have been recorded.

Pathological Appearances of the Liver.—The surface of the liver may show recent inflammation and adherent fibrin over the abscess, or, when the process is of some duration, fibrous adhesions uniting it to the diaphragm, abdominal wall, or adjacent viscera. These are most frequently met with between the convexity of the right lobe and the diaphragm; the abscess may then project upwards under the dome of the diaphragm and give rise to comparatively little enlargement of the liver in a downward direction.

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* Lafleur: Allbutt's System of Medicine, vol. iv, p. 156.

† Cantlie, J.: Brit. Med. Journ., 1899, vol. ii, p. 646.

‡ Davidson: Allbutt's System of Medicine, vol. iv, p. 141.

§ Godlee, R. J.: Medico-chirurg. Trans., vol. lxxxv, p. 119, 1902.

In its earliest stage a liver abscess appears as a pale, softened area, sometimes irregular in shape from the union of two or more such foci. This condition of commencing suppuration if aspirated may be recognized by finding cylinders of liver cells in the blood-stained material withdrawn, which, however, has no naked-eye resemblance to pus. The softened areas break down into recent abscess cavities which have ragged walls lined by necrosing liver tissue. Immediately around the spreading abscess the liver substance is softened, buff-colored from swelling, degeneration, and necrosis of the liver cells and infiltration with polymorphonuclear leucocytes. The vessels contain emboli of pyogenic cocci. As the inflammatory change spreads outwards it may set up suppurative thrombosis in the portal spaces and thus give rise to foci of suppuration in the neighbourhood, which may eventually open into the original abscess.

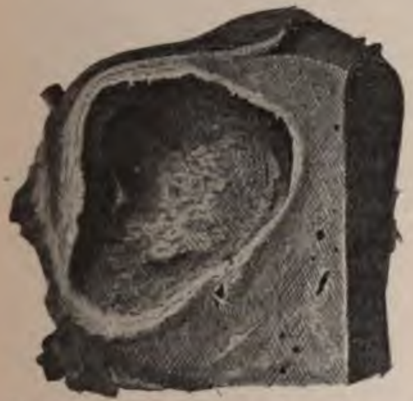

Fig. 20.—Single Abscess with a Definite Capsule.

A glass rod shows where it ruptured into the inferior vena cava. From a specimen (series ix, 171m) in St. George's Hospital Museum. (Drawn by L. Jones, M.B., F.R.C.S.)

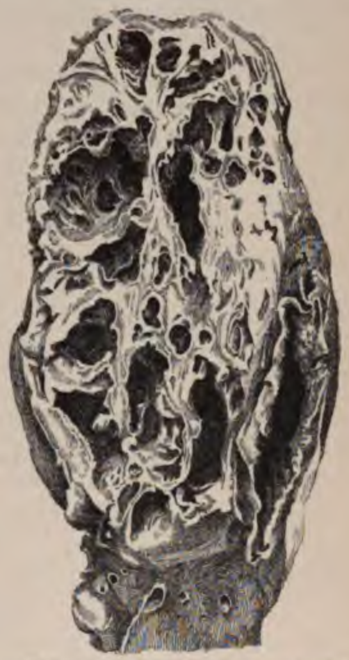

Fig. 21.—Section of the Right Lobe of the Liver, showing the Union of a Number of Separate Abscesses into an Areolar Abscess Cavity.

From a specimen (series ix, 171c) in St. George's Hospital. (Drawn by Dr. E. A. Wilson.)

In an abscess of some standing there is lining of granulation tissue, which is ragged at first, and later becomes smooth. Outside this there is a fibrous capsule which runs into and invades the surrounding liver substance for a short distance. The internal lining of granulation tissue may have débris and fibrin adherent to it, and often shows necrosis on the internal surface. The granulation tissue contains newly formed vessels and in its deeper layers shows developing fibrous tissue. In this way a capsule is formed, which in old abscesses is of considerable extent and is formed of dense, well-formed fibrous tissue. This fibrous tissue invades the liver for a short distance and passes between the liver cells, which are flattened and often spindle shaped, so as to suggest the view, now known to be erroneous, that they become transformed into fibrous tissue.. The liver cells proliferate and give rise to columns of small cubical cells,—the so-called new bile-ducts,—and as a result the developing fibrous capsule around an abscess of some duration contains altered liver cells and pseudo-bile canaliculi. In old abscesses the capsule is often pigmented and may undergo calcareous infiltration. Occasionally suppurating foci are found outside the comparatively well-formed wall of a single abscess.

The rest of the liver is usually enlarged, and after evacuation of the abscess heavier than in health. In 132 cases tabulated by Waring this was the condition of the organ in 113. The increase in size is chiefly due to parenchymatous inflammation and cloudy swelling, but, in addition, compensatory hypertrophy of the remainder of the liver occurs. In chronic cases where a fistula has existed increase in size of the liver may be due to lardaceous disease. In some instances there may, in addition, be pylephlebitic abscesses in the substance of the liver. In rare instances the liver substance may have a striking appearance, being of a bright yellow colour and firm consistence, resembling the appearances seen in phosphorus poisoning.

I met with this appearance in a case of a loculated liver abscess due to infection derived from the appendix, which contained a pin.* In St. Bartholomew's Hospital Museum there is a specimen (2196D) of multiple abscess showing this appearance. E. J. Waring† in 113 fatal cases mentions one where the liver had this aspect.

The scars of former abscesses that have been opened are sometimes seen. Abscess is very rarely found in a genuinely cirrhotic liver; in Waring's 113 cases the rest of the liver was cirrhotic in two.

In the so-called *amœbic abscesses* of the liver the histological appearances described are so peculiar that special reference must be made to them. In small and recent abscesses there is a glairy, translucent fluid, which when removed leaves a shreddy, spongy wall. The wall is irregular from the remains of the portal canals, which are left by the necrosis and disintegration of the surrounding liver cells. The liver cells undergo necrosis probably as the result of the action of toxic substances manufactured by the amœbæ, and then liquefy and disintegrate. Amœbæ are found in the capillaries in the immediate neighbourhood of the abscess.

There is a remarkable absence of leucocytic massing in the neighbourhood of the small abscesses which is quite characteristic (Lafleur ‡). The process is one of colliquative necrosis rather than of inflammation. Rogers,§ however, who regards the small multiple amœbic abscesses as due to a mixed infection of amœbæ and pyogenic cocci, figures small-cell infiltration in these minute abscesses.

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* Trans. Path. Soc., vol. xlix, p. 106.

† E. J. Waring: Abscess of the Liver, p. 137.

‡ Lafleur: Allbutt's System of Medicine, vol. iv, p. 158.

§ Rogers, L.: Brit. Med. Journ., 1903, vol. i, p. 1318.

Large chronic amœbic abscesses differ little from the appearances in other chronic hepatic abscesses. Amœbæ are much less numerous than in the recent small amœbic abscesses, but are found in the same situation, viz., in the wall of the abscess cavity.

Contents of the Abscesses.—In large abscesses the character of the pus may vary very considerably; it may be white and creamy, yellow, brownish red or chocolate colour, green; thick, mucoid, or even serous. The red colour is due to admixture with blood and the remains of the liver tissue. In amœbic abscess the contents of the smaller abscesses are translucent, glairy, and do not flow easily. In larger amœbic abscesses the fluid is very viscid and does not resemble ordinary pus.

Microscopically the amœbic abscesses contain amœbæ, which are naturally more numerous in the recent abscesses, necrosing liver cells, and red blood-corpuscles. Very few leucocytes are present and the contents thus differ markedly from ordinary pus. Charcot-Leyden crystals have been found. (Kruse and Pasquale.[*]) Amœbic abscesses may also contain various kinds of micro-organisms, such as streptococci, staphylococci, Bacillus coli. The pus is said to have a mawkish taste, and is not, as a rule, offensive. In abscesses on the under surface of the liver in contact with the bowel the contents may have a very fæcal odour, due probably to secondary infection with members of the colon group.

Bacteriology.—Hepatic abscesses may be divided into (i) those which contain amœbæ—called dysenteric by Kartulis; and (ii) the non-amœbic, due to micro-organisms, usually absorbed from the alimentary tract, and termed by Kartulis idiopathic.

Amœbæ.—Since the discovery of amœbæ in dysentery and in hepatic abscesses, some uncertainty has naturally arisen as to what proportion of the cases of tropical liver abscesses are due to this cause and to what extent amœbæ are concerned in the production of suppuration.

The Amœba coli described in 1875 by Lösch in dysenteric dejecta and by Kartulis of Alexandria in 1887 in the contents of an hepatic abscess, is a unicellular, motile organism. It varies in size, its diameter being from 6 to 35 μ, more commonly between 12 and 26 μ. It has a nucleus which stains badly, and has an outer layer or ectoplasm and a larger and inner portion—entoplasm. Its pseudopodial movements cease when the temperature falls below 75° Fahr., hence when stools or pus are examined microscopically for amœbæ, a warm stage is necessary.

The causal relation of amœbæ to the amœbic abscesses of the liver has given rise to a considerable amount of discussion, and the question is very far from being settled. The following views have been held.

(1) Kartulis,[†] who first recognized amœbæ in the pus of liver abscesses, believed that they played an important accessory part in the production of abscesses, by conveying pus-producing micro-organisms to the liver and by rupturing the hepatic capillaries by their active move-

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[*] Kruse and Pasquale: Zeitschrift f. Hyg., Bd. xvi, 1894. Quoted by Lafleur, Allbutt's System of Medicine, vol. iv, p. 154.

[†] Kartulis: Centralblatt f. Bakt., Bd. ii, 1887. Virchow's Archiv, Bd. cxviii, 1889.

ments; the production of pus not being due to amœbæ, but to the pyogenic micro-organisms.

(2) Kruse and Pasquale regarded the disintegration of the liver and abscess formation as due to a direct co-operation of the amœbæ with micro-organisms.

(3) Councilman and Lafleur[*] believe that the amœbæ alone are responsible for the abscess, since in the smallest abscesses bacteria are absent while amœbæ are plentiful. In larger abscesses bacteria are not numerous, and the lesions are not like those produced by bacteria. These lesions are largely necrotic, and are thought to be due to a soluble toxine manufactured by the amœbæ.

(4) It has been suggested by Miss Sheldon Amos[†] that the presence of amœbæ in liver abscesses is a secondary infection and that the amœbæ only gain a footing in the liver when it has been damaged by bacterial invasion. This view is supported by the fact that amœbæ are absent from cerebral abscesses in cases where they are found in the pus from the liver. Kelsch and Nimier[‡] deny that amœbæ are responsible for the production of liver abscess; and there is rather a tendency at present to doubt the importance of amœbæ as factors in the production of hepatic abscess, even though they may be found in the pus. L. Rogers,[§] from observations in Calcutta, has recently endorsed Councilman and Lafleur's view that amœbæ alone give rise to large hepatic abscesses, and in the view that amœbæ may work their way from the bowel across the peritoneum to infect the surface of the liver.

When an abscess is opened, amœbæ may not be found in the pus until some days have elapsed; this has been explained by the fact that the amœbæ are chiefly found in the walls of the abscess and not in its contents. In hepatic abscesses examined in England, Manson[‖] has found amœbæ in considerably over 50 per cent.

Bacteria.—In non-amœbic cases examination of the pus bacteriologically shows discordant results. In some instances the pus is sterile; this has been explained by supposing that in chronic cases the micro-organisms originally present have died out. Pus-producing micro-organisms have frequently been found, such as the Staphylococcus pyogenes aureus, albus, citreus, and streptococci. Typhoid bacilli have been found in pure culture (Cassuto[**]) or in combination with other micro-organisms. Ordinary pneumococci, Friedländer's pneumobacillus, Bacillus pyocyaneus, and the colon bacillus are also sometimes present.

Condition of the Pleura.—Inflammation of the pleura is a very common occurrence in hepatic abscess; it may be due to a spread of infection along the lymphatics and may be dry, serous, or purulent. Pleurisy may give rise to universal adhesions and so prevent the abscess rupturing into the pleura, but thus favour its rupture into the lung. An empyema due to this course may, as in Duplant's case, be encysted between the lobes of the lung. Rupture or direct leakage of an abscess into the pleura will give rise to a large empyema. This will be referred to later.

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[*] Councilman and Lafleur: Johns Hopkins Hosp. Reports, vol. ii, 1891.

[†] Miss Sheldon Amos: Journ. Path. and Bacteriolog., vol. viii, p. 346, 1902.

[‡] Kelsch and Nimier: Bull. Acad. de Méd. Paris, 1900, t. xliii, p. 237.

[§] Rogers, L.: Brit. Med. Journ., 1902, vol. ii, p. 844; 1903, vol. i, p. 1315.

[‖] Manson: Tropical Diseases, p. 456, 1903.

[**] Cassuto: Thèse de Paris, 1900.

Condition of the Lungs.—The lower lobe of the right lung may be compressed by the upward pressure of the liver and diaphragm, or by a pleural effusion; or if it is adherent to the diaphragm it may become inflamed from direct extension of inflammation from the abscess through the diaphragm or the abscess may burst into the lung. In cases where the abscess has leaked into the hepatic veins or into the inferior vena cava there may be secondary pyæmic abscesses in the lungs. The rupture of an hepatic abscess into the lung will be referred to later.

CLINICAL PICTURE.

SYMPTOMS.

Latency; Onset; Fever; Sweating; Rigors; Pain; Shoulder Pain; Tenderness; Cough; Digestive Disturbances; Arthritis; Nervous Disorders.

There is very great variety both in the individual symptoms and also in their association; this is shown by the number of conditions for which hepatic abscess has been mistaken. (*Vide* Diagnosis.) Very frequently the symptoms suggest rather than definitely point to the presence of hepatic abscess.

Latency.—An abscess may remain perfectly latent and only be found at death; according to Rouis, this occurs in 13 per cent. In some cases there are no definite symptoms or signs until the abscess ruptures and rapidly brings about a fatal result.

The onset of symptoms is gradual, as a rule, and is ushered in by malaise, languor, and general debility, and the signs and symptoms of acute congestion of the liver and acute hepatitis. (*Vide* p. 117.) Indefinite malaise may precede by many weeks any definite evidence of abscess. In some instances there is an acute onset with shivering or a rigor, and the condition may imitate pneumonia of the right lower lobe.

Fever is perhaps the most constant sign of hepatic abscess. The temperature varies. It may be continuous at first, then remittent, and in the later stages intermittent. It may closely imitate malaria, or be extremely irregular. In chronic cases the temperature may be normal, while in severe and advanced forms of the disease it may be low and even abnormal.* In exceptional instances there may be little or no fever, even with a large and recent abscess. Cases have been met with in which there is an absence of pyrexia from start to finish.

Moir † records a case where the abscess contained 70 ounces of pus while the temperature ranged between subnormal and 99°.

Sweating.—Nocturnal sweats may be very profuse. Perspiration often occurs during the day when the patient drops off to sleep. In fact, the sweating is more related to sleep than to the night hours, and is chiefly nocturnal because sleep is more general then.

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* Smith, Johnson: Brit. Med. Jour., 1900, vol. ii, 550.

† Moir, D. M.: Indian Med. Gaz., June, 1897.

Rigors are often met with in the course of the disease. In some cases there is a single rigor at the onset or early in the course of the disease; in others there are frequent rigors, while again they sometimes only come on towards the end of the case. A feeling of chilliness often accompanies the evening rise of temperature.

Pain over the liver and a sense of fulness in the right hypochondrium are very commonly present. Though pain may be present from the start of suppuration, it is much more in evidence when the abscess is large and approaching the capsule of the liver, than early in the process or when the abscess is deeply situated. The pain may be constant and dull, probably from increased tension inside the liver; this is usually early in the course of the disease, or intermittent and sharp and stabbing, and, like pleuritic pain, brought on by respiratory movements. It may be actually due to pleurisy or to inflammation of the capsule of the liver, and is then rather a late symptom. Pain on swallowing, due to food disturbing the liver, as it enters the stomach, is mentioned by Manson.[*]

Shoulder Pain.—In abscess, as in some other affections of the liver, pain may be referred to the shoulder, and may be felt over the scapula or at the tip of the acromion process. It has been suggested that this localization may depend on the communication between the nerve to the subclavius muscle and the phrenic nerve. According to Manson,[†] it occurs in about one-sixth of the cases. It is most frequently present when the abscess is in the upper part of the right lobe. In cases of abscess in the left lobe the pain may be referred to the left shoulder. In very rare instances the pain is bilateral. (E. J. Waring.[‡])

Tenderness.—On deep palpation or percussion tenderness of the liver is generally elicited. Localized tenderness over some part of the surface of the liver is perhaps the least unsatisfactory sign of hepatic abscess.[§] By methodical palpation over the liver a localized tender spot may be found which serves as a useful guide to the position of the abscess. Occasionally vomiting is constantly induced by pressure on one spot. (Smits.[‖])

Cough.—In hepatic abscess there is often a spasmodic, hacking cough, which is usually worse at night, and may be ineffectual or unaccompanied by sputum. It may be due to irritation of the pleura over the diaphragm, to actual pleurisy, or possibly merely to reflex irritation from the liver. It is not peculiar to liver abscess. When the abscess discharges through the lung, severe cough comes on and expectoration may be copious. As much as 4 pounds of pus has been brought up in twenty-four hours.[**] The colour of the expectorated matters differs greatly in different cases; it may be mixed with bile. In amœbic abscesses amœbæ may be found in the sputum before the abscess has burst into the lung.

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[*] Manson, P.: Tropical Diseases, Ed. i, p. 353.

[†] Manson, P.: Tropical Diseases, p. 448, 1903.

[‡] Waring, E. J.: Abscess of the Liver, p. 147.

[§] Smith, Johnson: Brit. Med. Journ., 1900, vol. ii, p. 550.

[‖] Smits: Archiv f. klin. Chirurg., Bd. lxi, S. 173, 1900.

[**] Waring: Abscess of Liver, p. 153.

Digestive Symptoms.—*Vomiting* appears to be more frequent when the abscess is in the left lobe or when there is an abscess in the left lobe together with one in the right. In very rare instances vomiting may be due to the abscess pressing on the pylorus and leading to pyloric obstruction. Maclean * described pyloric obstruction due to hepatic abscess. *Appetite* is poor or completely lost, as a rule, but sometimes it is well preserved. *Flatulence* may be troublesome.

There may be constipation, diarrhœa, or the two may alternate. Septic absorption from the abscess may give rise to ulceration of the intestine and diarrhœa. A recrudescence of a former dysentery is not uncommonly described; while in some cases there may be a continuance of chronic dysentery. When the abscess bursts into the alimentary tract, large quantities of pus may appear in the stools. In rare cases there may be considerable hæmorrhage from the bowel.†

Captain Weston, R. A. N. C., has told me of a case where there were profuse hæmorrhages from the bowels apparently due to an abscess in the quadrate lobe of the liver pressing on the portal vein.

Arthritis, etc.—Swelling and painful enlargement of the joints, presumably due to toxic products absorbed from the liver abscess, may occur, just as in dysentery. They may be pyæmic, but are probably usually toxic; at any rate, they tend to disappear when the abscess is opened or discharges.

It is interesting to note that Girard‡ observed clubbing of the fingers in a case of hepatic abscess in which there were no pulmonary lesions. It is possible that, like arthritis, this change was of toxic origin.

Nervous Symptoms.—As in most hepatic diseases, there is a good deal of irritability or mental depression, which may even become so marked as to pass into melancholia. Insomnia is very common. The mental disturbance may be referred to the action of poisons on the cerebral cortex. The poisons may be absorbed from the liver abscess or may be derived from the alimentary tract, the liver being unable to deal with them. Cerebral symptoms may in rare instances depend on pyæmic abscesses in the brain or on septic meningitis. In the terminal stages delirium, or in rare instances convulsions, may occur before death.

PHYSICAL SIGNS.

Wasting; Decubitus; Facial Aspect; Jaundice; Pulse; Blood; Respiratory System; Abdominal Signs—Painful Succussion—Skiagraphy—Rigidity of Right Rectus Muscle—Ballottement—Hepatic Dulness—Friction; Œdema of Feet; Urine.

Wasting.—Loss of flesh is progressive and may be very considerable. The degree of wasting necessarily depends on the duration and intensity of the disease and the size of the abscess. In rare instances weight may actually be put on while an abscess is maturing. (Osler.*)

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* Maclean: Brit. Med. Journ., April 1, 1874.

† Haasler: Deutsche med. Wochen., Jan. 16, 1902.

‡ Girard: La Semaine Médicale, 1903, p. 32.

Decubitus, or the position assumed by the patient, is generally dorsal or right-sided, as being that in which there is greatest freedom from pain. When lying on the back, the chest is raised and the knees are somewhat flexed. When the patient turns onto the left side, the liver tends to fall away from the wall of the abdomen on the right side and pain is frequently felt. This is probably due to stretching of adhesions or to the separation of the inflamed capsule of the liver from the parietal peritoneum. On the other hand, the patient is sometimes more comfortable on the left side. The differences in the position assumed by the patient may depend on the increased size of the liver and on existence of adhesions. Thus, when the liver is greatly enlarged the right-sided position is most comfortable, but if there are peritoneal adhesions in certain situations, the right-sided position may give rise to tension on them and so to pain.

Facial Aspect.—The complexion is pale or sallow with a muddy tint, and often slightly icteric. The conjunctivæ if not jaundiced are often of a waxy, white colour. The expression is one of anxiety and worry, the eyes are often sunken, and the general aspect, which is more easily recognized than described, may be peculiarly suggestive of the disease. The skin in the early stages may be hot and dry, but later it becomes moist and clammy.

A remarkable diffuse cyanosis for which there was no satisfactory explanation was noticed by Osler† in one case.

The tongue is usually furred along the centre with a red tip. A smooth red tongue with fissures running in all directions is not uncommon. A strong hepatic odour from the patient is described by Hatch‡ as a sign of hepatic abscess; probably it is present only when the abscess is of considerable size.

Jaundice.—Marked jaundice is very rare; a slight degree, probably due to local catarrh of intra-hepatic ducts near the abscess, and tingeing the conjunctivæ is sometimes present.

Definite jaundice was seen in 58 out of 375, or in 16 per cent., cases quoted by Thierfelder.§

In exceptional cases an abscess may exert pressure on the extra-hepatic ducts in the portal fissure.

In a case reported by Moir‖ a huge abscess compressed the common hepatic duct.

The pulse is of low tension, full, and somewhat quickened—80 to 100. Exceptionally it is slowed.

The blood may show leucocytosis, and when this is so, is of great service in distinguishing hepatic abscess from malaria or typhoid fever. The existence of considerable leucocytosis—30,000 to 50,000 per cubic millimeter—has led to the detection of abscess in patients formerly the subjects of dysentery (Boinet *) or thought to have malaria (Rogers †). When leucocytosis is present, it is said to be constant (Boinet), and not to appear and disappear as it does in intermittent hepatic fever. The leucocytosis is an ordinary polymorphonuclear one, 70 to 80 per cent. of the leucocytes being of this nature. Leucocytosis, though highly suggestive of hepatic abscess, is by no means found in all cases of abscess. When septic absorption is prevented by a thick capsule and in amœbic cases there may be no leucocytosis. It has been thought that leucocytosis is most marked in small, deeply seated abscesses, and less in large abscesses bulging on the surface of the liver. (Rogers.)

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* Osler: Medical News (U. S. A.), April 12, 1902, p. 673.
† Osler: Medical News (U. S. A.), April 12, 1902, p. 673.
‡ Hatch: Brit. Med. Journ., 1900, vol. ii, p. 1374.
§ v. Ziemssen's Cyclopædia of Practical Medicine, vol. ix, p. 126.
‖ Moir: Indian Med. Gaz., Oct., 1902, p. 391.

It was absent, or practically so, in three out of five cases recorded by Osler.‡ It was absent in a case examined by Cabot,§ and Rispal‖ failed to find more than a slight leucocytosis (15,000 per cubic millimeter) in three cases.

Respiration is shallow and chiefly thoracic, since movement of the abdomen may be attended with pleuritic pain. The rhythm is more rapid than normal, both because of the fever and on account of the shallow respirations. In cases of amœbic abscess the organisms may be found in the expectoration.

Lung Signs.—Compression of the lower lobe of the right lung is common and may show itself by crepitations and dulness. When inflammation has spread through the diaphragm to the pleura, friction may be heard. Hepatic abscess is therefore very likely to imitate pneumonia or empyema at the right base; the occurrence of signs of right-sided pleurisy in a patient who has had dysentery should always suggest the possibility of an abscess of the liver. The appearance of pleural friction in a case thought to be one of hepatic abscess is a sign that extension of the inflammatory process to the thorax is in process, and is therefore a signal for operative interference, so as to prevent rupture of the abscess into the pleura or into the lung. But in some cases of acute hepatitis which have been fruitlessly explored and have recovered some friction at the base of the right lung may have been present.

An empyema may follow hepatic abscess in several ways. The abscess may burst directly into the pleura or the infection may spread through the diaphragm, or pus may travel by the blood-stream into branches of the pulmonary artery and set up abscess formation in the lung with the secondary production of an empyema. An empyema may form between the lobes of the lung and give rise to great difficulty in its evacuation.

Rupture of an hepatic abscess into the lung may give rise to the signs of a cavity in the lower lobe, which, according to Godlee,** are most commonly met with below and to the inner side of the right nipple, but may be present posteriorly. When a pulmonary abscess consequent on an hepatic abscess is diagnosed, no time should be lost in operating upon it, so as to prevent extensive destruction of the lung.

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* Boinet: Soc. de biolog., Paris, Dec. 29, 1900.
† Rogers, L.: Brit. Med. Journ., 1902, vol. i, p. 831; and 1902, vol. ii, p. 844.
‡ Osler: Medical News (N. Y.), April 12, 1902, p. 673.
§ Cabot: Clinical Examination of the Blood, p. 253
‖ Rispal: Compt. rend. Soc. de biolog., 1901, p. 862.
** Godlee: Medico-chirurg. Trans., vol. lxxxv, p. 119, 1902.

The abdomen is full and somewhat distended; sometimes the distension is general, as if from tympanites. There is often definite fulness or bulging in the right hypochondrium or epigastrium, and sometimes a rounded projection in the position of, or in connexion with, the liver may be seen to move with respiration. Fluctuation in some cases can be made out over the tumor. When an abscess is situated near the middle line of the body it may pulsate from the transmission of impulses from the aorta.

Carpenter* describes a painful swelling the size of a fœtal head pulsating visibly, but not expansile; operation showed it to be an hepatic abscess containing two pints of pus.

Bulging of the chest on the right side as compared with the left, and in some cases protrusion and widening of the intercostal spaces, may be seen. Redness of the skin or localized œdema indicates that an abscess is in close contact with the affected cutaneous area. Though a very valuable sign, œdema over the abscess is only present in about 5 per cent. of the cases. (Stevenson.†) When the abscess is very large, it may fill the greater part of the abdomen, and has given rise to an erroneous diagnosis of ascites. Marked ascites is an extremely rare accompaniment of hepatic abscess.

Painful Succussion.—If the patient is shaken, much in the same manner as in obtaining "Hippocratic succussion" in pyo-pneumothorax, pain is felt in the liver which may spread to the right shoulder, the pit of the stomach, across the abdomen, or to the right iliac fossa, according to the situation of the abscess. Malbot‡ considers this a certain sign of abscess.

Skiagraphy has been applied to the detection of hepatic abscess.§ In health the shadow cast on the screen shows that the right leaflet of the diaphragm is 1½ inches above the level of the left leaflet and is constantly moving with respiration. In cases of abscess it is displaced upwards and does not move.

Rigidity of the upper part of the right rectus muscle may certainly occur when an abscess is present, but it is far from constant; moreover, it is met with in other conditions, such as inflammation of the gall-bladder, disease of the pylorus, duodenal ulcer, or inflammation of the muscle itself, and therefore cannot be considered as a sign of any very special value. The rigidity of the rectus may considerably interfere with the examination of the liver. Dalton ‖ refers to a case in which the rigidity did not relax under an anæsthetic.

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* Carpenter: Brit. Med. Journ., 1899, vol. ii, p. 208.

† Stevenson: Lancet, 1898, vol. ii.

‡ Malbot: Archiv général de Médecine, August, 1899, p. 179.

§ Loison: Rev. de Chirurg., 1900, p. 522.

‖ Dalton, N.: King's Coll. Hosp. Reports, vol. ii, p. 25.

Percussion, besides eliciting tenderness and causing pain, may convey to the examiner a sensation of **ballottement,** as if he was percussing a thick-walled elastic bag filled with air.*

Hepatic Dulness.—The area of hepatic dulness is increased both in an upward and in a downward direction. Though this is the rule, it is not without exception, and in some instances the underlying colon may mask the dulness which a collection of pus would naturally give rise to. The dulness in extreme cases may reach as high as the second rib. (Waring.†) As the abscess is usually in the right lobe, the enlargement is mainly on that side, and since the abscess is most frequently near the convexity of the liver, the enlargement is chiefly in an upward direction and not downwards, as in cirrhosis and in lardaceous and malignant disease. When the abscess is deeply situated, the whole lobe is expanded and enlarged, but later, when the abscess reaches the surface, it may give rise to a definite projection from the outline of the organ.

Friction due to perihepatitis, set up by the approach of the abscess to the surface of the organ, may be heard or sometimes even felt by the hand. There is commonly friction over the base of the right lung, due to pleurisy set up by the spread of infection along the lymphatics of the diaphragm.

Fine crepitation, like that obtained by pressing on frozen snow, may be heard over the liver; it occurs with inspiration and expiration. Bertrand regarded it as due to perihepatitis, but Hassler and Boison have heard it in cases where laparotomy showed that there was no perihepatitis, and believe it is produced in the softened and œdematous liver substance around the abscess.

The **spleen** is rarely enlarged. This is of importance in distinguishing abscess from malaria.

Œdema of the feet often occurs late in the course of the disease.

The urine is high-coloured and may be of a high specific gravity, and loaded with urates. When considerable destruction of the hepatic substance has taken place, the amount of urea may be diminished. Indican may occur. Albuminuria is sometimes present. From absorption of pus albumose may be found in the urine; but it has been absent in the cases I have seen.

In a case of abscess following dysentery crystals of leucin, tyrosin, and cholesterin were present in the urine for ten weeks; on opening the abscess the urine became normal.‡ Crystals resembling tyrosin, but really composed of a soap of lime and magnesium, were found in one case by Pfähler.§

COURSE AND DURATION.

The abscess may remain latent until it ruptures and gives rise to acute symptoms or is revealed by a discharge of pus from the alimentary or respiratory tract. It is difficult to say when hepatitis passes into suppuration, and therefore to estimate precisely the duration of an abscess in the liver. An abscess may run its course in three weeks or, if it gives rise to a fistula, especially in connexion with the lungs, may drag on for many months.

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* Hassler and Boison: Rev. de Méd. Oct., 1896.
† Waring, E. J.: Abscess of the Liver, p. 149.
‡ Lancet, 1900, vol. ii, p. 1729.
§ Pfähler: New York Med. Journ., Feb. 15, 1902.

TERMINATION.

If not operated upon, an hepatic abscess may either remain intact or may rupture into some neighbouring cavity or viscus. An abscess which remains intact may in rare instances tend to dry up and become shut off and encysted, giving rise to a caseous mass surrounded by a fibrous capsule. How often this actually occurs it is difficult to say, inasmuch as an abscess cannot be certainly diagnosed until it has reached a considerable size, and would then be operated upon.

In 25 cases in which recovery took place, there were fair grounds for believing that the abscess underwent this spontaneous cure in two. (E. J. Waring.*)

Possibly this spontaneous cure is even less frequent than is sometimes thought, since some so-called "receding" abscesses found postmortem may in reality have been gummata. If the abscess remains intact and does not discharge its contents spontaneously, it usually leads to death.

In 300 fatal cases tabulated by Waring in 1854, 48, or 16 per cent., only were operated upon, while 169, or 56 per cent., died with the abscess intact.

Though the abscess practically remains intact, it may give rise to secondary abscesses in the lungs and to general pyæmia. Death may be due to detachment of a thrombus formed in one of the hepatic veins and pulmonary embolism. In some cases the destructive suppurative change in the lungs may give rise to fatal hæmoptysis. As a rule, the fatal result is due to septicæmia, septic absorption, and exhaustion. Diarrhœa or an apparent recurrence of dysentery may carry the patient off. In rare cases death may be directly due to intestinal hæmorrhage; this has been observed by Hassler† and Duplant.‡

RUPTURE.

If undetected or not operated upon, an hepatic abscess may rupture internally, or in very rare instances onto the surface of the body. The percentage of cases in which rupture occurs depends on the diagnosis and on the frequency with which operative measures are undertaken. In 563 cases of hepatic abscess collected by Cyr, 83, or 15 per cent., only were operated upon, and rupture occurred in 159, or 28.6 per cent. But it must be remembered that interesting examples of perforation of hepatic abscess are more likely to be put on record than more commonplace cases where the abscess is operated upon or not detected. More than half the cases of perforation, as will be seen from Cyr's and Thierfelder's tables, were in an upward direction—through the diaphragm.

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* Waring, E. J.: Abscess of the Liver, p. 195.
† Hassler: Deutsche med. Wochen., 1902.
‡ Duplant: Lyon Médical, Jan. 26, 1902.

	Cyr,* 159 Cases.		Thierfelder,† 170 Cases.	
Lung	59	57 per cent.	74	59 per cent.
Pleura	31		26	
Pericardium	1		4	
Peritoneum	39		23	
Stomach	8		13	
Intestines	13		32	
Kidney	2		1	
Inferior vena cava	3			
Bile passages	4			
Externally	2			

In both these two series perforation occurred in two positions in three cases, so that the numbers of the perforations exceed the number of cases.

The various situations in which rupture occurs may conveniently be considered seriatim under the following heads: rupture into—(1) Lung, (2) Pleura, (3) Pericardium, (4) Peritoneum, (5) Stomach and duodenum, (6) Intestines, (7) Gall-bladder and bile-ducts, (8) Kidney, (9) Hepatic veins and Inferior Vena Cava, (10) Portal Vein, (11) Onto the surface of the body.

(1) **Rupture into the Lung.**—This is the most frequent method by which an hepatic abscess spontaneously discharges. In an overwhelming majority of cases it is the right lung into which the abscess opens. Before the abscess can extend into the lung the liver must become adherent to the diaphragm, and the diaphragm to the base of the lung. The inflammatory processes necessarily give rise to pain and usually to signs of basal pleurisy and to cough. Inflammation spreads into the lung and consolidation with suppuration ensues; the communication between the abscess cavity in the liver and that in the lower lobe of the right lung is usually somewhat small, like a shirt-stud abscess, and may be missed; in some instances no naked-eye perforation of the diaphragm is forthcoming. In rare cases there may be a small collection of pus between the diaphragm and lung as well as an abscess in the lower lobe of the lung. The formation of an abscess in the lower lobe is, according to Lafleur, due to an extension of inflammation and infection by continuity from the liver, and not hæmatogenous and due to embolism through the pulmonary artery. On the other hand, amœbæ have been found in the small branches of the pulmonary artery, so that hæmatogenous infection is quite conceivable. The suppurative process in the lower lobe spreads into the surrounding pulmonary tissue and tends to produce fistulous passages in the lung, which as a result becomes much disorganized. The abscess discharges into one of the bronchi in the lower lobe of the lung and characteristic sputum mixed with blood is coughed up. The sputum contains pus, blood, and often fragments of hepatic and pulmonary tissue, fat globules, micro-organisms, and amœbæ. Occasionally a fistulous communication between the bronchi and a bile-duct in the liver may be established and bile may be brought up from the lungs.

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* Cyr: Traité Practique des Maladies du foie, 1887.

† Thierfelder: Cyclopædia of the Practice of Medicine, v. Ziemssen, vol. ix, p. 138.

The pulmonary abscess may progress, and, indeed, prove fatal from exhaustion or hæmoptysis, when the original hepatic abscess has undergone complete cure. Since the pus is like that brought up from the liver and may contain amœbæ, the expectoration of chocolate-coloured pus does not prove that the original liver abscess has not healed. (Godlee.*) Lafleur,† writing on amœbic abscess of the liver, gives a very unfavorable prognosis in cases of rupture into the lung. Other writers, however, take a very different view; Decastro,‡ for example, estimating that recovery occurs in 76 per cent. of the cases.

(2) **Rupture into the Pleura.**—Rupture into the pleura, though much the same process, is less frequent than rupture into the lung. This depends on the fact that the abscess as it advances through the diaphragm tends to set up adhesive pleurisy and so glues the lower lobe of the lung to the diaphragm. When the abscess opens into the pleura, the signs are those of an empyema. The effusion may reach a very large size with great rapidity and seriously endanger the patient's life.

(3) **Rupture into the Pericardium.**—Rupture into the pericardium is very rare, since this is likely to occur only when the abscess is in the left lobe of the liver—a rare situation.

Waring § quotes 6 recorded cases and I have notes of 9 others, making 15 in all. In a very remarkable case recorded by Bentley ‖ there were four pints of sero-purulent fluid in the pericardium which communicated with an abscess in the left lobe of the liver.

An abscess in the left lobe may leak onto the surface of the liver and set up a subphrenic abscess which may subsequently perforate into the pericardium. Tolot** reports a case of this kind. The clinical evidence of rupture into the pericardium is severe pain, dyspnœa, and the rapid development of a pericardial effusion. Death follows very soon after this accident.

(4) **Rupture into the Peritoneum.**—This is a comparatively common form of rupture. It may occur freely into the general peritoneal cavity or may give rise to a localized intraperitoneal abscess which may subsequently burst into the general cavity of the peritoneum or may discharge into the bowel or even externally. Rupture of an abscess into the general cavity of the peritoneum may be due to traumatism or to muscular exertion, while the danger of leakage must always be borne in mind when the question of aspiration with a trocar through the abdominal wall is contemplated. Perforation into the general peritoneal cavity is more likely to follow sudden exertion or traumatism than to occur spontaneously, as an abscess pointing on the surface of the liver tends to set up local peritonitis and adhesions before actually rupturing. When rupture occurs into the general cavity of the peritoneum there

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* Godlee: Medico-chirurg. Trans., vol. lxxx, p. 119, 1902.

† Lafleur: Allbutt's System, vol. iv.

‡ Decastro: Des abscess du foie des Pays Chauds, Paris, 1870. Quoted by H. J. Waring: Diseases of Liver.

§ Waring, H. J.: Abscess of the Liver in the East Indies, 1854, p. 133

‖ Bentley: Trans. Path. Soc., vol. ii, p. 70.

** Tolot: Lyon Médical, 1902, p. 51.

are symptoms of severe collapse, and if the patient survives long enough, acute septic peritonitis results, which is nearly always fatal. In cases where the existence of an hepatic abscess has not been recognized, the sudden onset of acute symptoms may imitate perforation of an intestinal ulcer in ambulatory typhoid fever.

A soldier aged twenty-seven years who had contracted dysentery in the Transvaal War of 1900 was admitted into St. George's Hospital in a moribund condition. At the autopsy he was found to have several pints of turbid fluid in the peritoneal cavity and general peritonitis due to leakage from an abscess in the left lobe of the liver. The ruptured abscess was thin-walled and quite small, it communicated with a large abscess the size of a fœtus' head, which occupied the whole of the left lobe of the liver, and had walls composed of glistening fibrous tissue about ½ inch thick. The right lobe of the liver was greatly scarred from cicatrices but did not contain any gummata; it showed early lardaceous change. The portal vein was thrombosed; there had probably been ascites before the onset of acute peritonitis.

Hulke * has recorded a remarkable example of recovery from rupture of a hepatic abscess into the general peritoneal cavity which was flushed out some twenty-four hours after rupture occurred. In this patient an hepatic abscess had previously ruptured through the lung, and rather more than a year after recovery from the operation for rupture into the peritoneum, a third abscess in the liver was successfully operated upon.

(5) **Rupture into Stomach and Duodenum.**—When rupture occurs into the stomach or duodenum pus is vomited, sometimes in very considerable quantities, and is passed by the bowel, but from the distance which it has to travel the pus may not be detected in the fæces. After rupture the size of the liver may be perceptibly diminished, and in some instances a tympanitic note has resulted from entrance of air into the abscess cavity. The rupture into the stomach is preceded by dyspepsia and discomfort, and accompanied by vomiting and severe epigastric pain.

(6) **Rupture into the Intestines.**—An hepatic abscess very seldom opens into any part of the small intestine except the duodenum. Rupture into the colon is not uncommon; it is accompanied by colicky pain and a feeling of collapse and is followed by the passage of pus by the bowel

(7) **Rupture into the Gall-bladder or Bile-ducts.**—This is a very rare event. The pus may pass down the common bile-duct into the duodenum and so imitate rupture of an abscess into the bowel. Symptoms of biliary colic have been noted in this rare form of fistula.

(8) **Rupture into the pelvis of the right kidney** is very rare. H. J. Waring † estimates the recorded cases at about 10.

(9) **Rupture into the Hepatic Veins and Inferior Vena Cava.**—From the fact that the hepatic veins are not surrounded by any fibrous sheath at all comparable to Glisson's capsule around the portal canals, an hepatic abscess is more likely to leak or rupture into them than into the branches of the portal vein. The abscess may burst into one of the hepatic veins quite close to the inferior vena cava. In a few cases an hepatic abscess has been found to perforate directly into the inferior vena cava and not into the hepatic veins.

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* Hulke: Medico-chirurg. Trans., vol. lxxvi, p. 81.

† Waring, H. J.: Diseases of the Liver, p. 98.

Cyr's list contains 3 cases, and since then Flexner * (1897) has given an account of two cases in which amœbic hepatic abscesses perforated the inferior vena cava. A case occurred in St. George's Hospital which is figured on page 131; the abscess occupied a third of the liver and had set up parietal thrombosis in the inferior vena cava. The pulmonary artery contained firm thrombi and there was pneumonic consolidation of the right lower lobe.

When the abscess begins to penetrate the wall of the hepatic veins or inferior vena cava parietal thrombosis may be set up, and thus for a time prevent the pus entering freely into the circulation, but eventually pus passes into the blood-stream and tends to give rise to secondary abscesses in the lungs. Detachment of a large piece of clot may give rise to pulmonary embolism.

(10) **Rupture into the Portal Vein.**—Rupture into the portal vein is extremely rare. Occasionally the abscess is in contact with the wall of the vein and sets up thrombosis in the vein which would prevent the contents of the abscess from passing into the vein.

(11) **Rupture Externally onto the Surface of the Body.**—A liver abscess is very seldom allowed to rupture spontaneously on the surface of the body, though it would do so in a certain number of cases if not anticipated. Most frequently the abscess points anteriorly, but occasionally it presents in the loin.

COMPLICATIONS.

Apart from manifest rupture hepatic abscess may give rise to secondary inflammation and suppuration, especially in the thorax. From the spread of inflammation through the diaphragm there may be a simple serous pleurisy on the right side. Infection may travel through the diaphragm and set up an empyema on the right side, which may be encysted between the lobes of the lung, as in Duplant's † case. Infection may spread through the diaphragm, produce pleurisy and adhesions between the base of the lung and the diaphragm, and then extend into the substance of the lower lobe, setting up pneumonic consolidation, in the middle of which an irregular abscess may develop. Rupture of the abscess into the lung and pleura and broncho-biliary fistula have already been described.

Cerebral Abscess.—One of the dangers of an empyema or a pulmonary abscess is that a cerebral abscess may follow.

Godlee ‡ describes an instructive case where the liver abscess was completely healed but there were numerous abscesses in the right lung and one as large as an orange in the left lung; death was due to an abscess in the right occipital lobe of the brain.

Abscesses in the brain which do not contain amœbæ may occur in cases where the hepatic abscess contained them; this is comparable to what sometimes occurs in actinomycosis, pyæmic abscesses only containing pyogenic cocci.

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* Flexner: American Journal of Medical Sciences, vol. cxiii, p. 553, May, 1897.

† Duplant: Lyon Médical, Jan. 26, 1902.

‡ Godlee: Medico-chirurg. Trans., vol. lxxxv, p. 119, 1902.

As a result of firm adhesions, associated with an old amœbic abscess in the left lobe of the liver, fatal **strangulation of the small intestine** has been recorded. (Rogers.[*]) From adhesions on the under surface of the liver around the portal fissure, in cases where an abscess has been successfully operated upon and contraction has followed, compression of, and traction on, the bile-ducts giving rise to jaundice, or on the colon or pylorus, producing kinking and dilatation of the stomach, may occur. (Godlee.[†])

Thrombosis of the inferior vena cava is a very rare complication; a parietal thrombus may form when an abscess bursts into the inferior vena cava, which itself is very rare.

In one case of hepatic abscess with extreme marasmus under the care of my colleague, Dr. Ewart, there was extensive thrombosis of the inferior vena cava, which appeared to have spread from the iliac veins; there was no focus of suppuration in the pelvis to account for it. In this instance there was some œdema of the feet and legs, but this may occur late in the course of hepatic abscess without thrombosis of the inferior vena cava.

Escape of bile from the fistula of the operation wound is not very uncommon, but it is rare for all the bile to pass in this way, as in three cases mentioned by Godlee.[‡]

Lardaceous disease may supervene as the result of long-continued discharge of pus from a fistulous passage, such as a hepato-bronchial fistula.

DIAGNOSIS.

There is no one sign or symptom which may not be absent in tropical abscess. The most frequent indications of liver abscess are pain in the region of the liver, progressive enlargement of the organ, and fever; but these may be present in congestion or acute hepatitis as well as in other conditions. The presence of a fluctuating swelling or œdema of the abdominal wall over the liver make the diagnosis almost certain, but unfortunately they are so often, or in the case of œdema generally, absent. The history that the patient has had dysentery or has been in tropical countries, the fact that the patient is manifestly ill, and the presence of some of the commoner signs and symptoms of abscess, such as hepatic pain, enlargement, and tenderness, and continued fever in the absence of any evidence of malaria or other sufficient cause, are strong grounds for suspecting a tropical abscess.

Boinet[§] has recently laid stress on the value of a considerable leucocytosis in cases where there is no other proof of abscess, but other observations show that the leucocytosis may be comparatively slight or absent. (Osler.[‖]) Leucocytosis in a doubtful case is in favour of abscess, but its absence does not exclude abscess.

Puncture of the liver with a fine trocar in order to determine whether pus is present, is a means of settling the diagnosis which is often employed. It is not, however, in spite of statements to the contrary, free either from fallacy or from danger. The trocar may, of course, miss the abscess or may pass through it, or may get blocked and not bring any pus away. Death has been known to follow exploratory puncture from hæmorrhage (Hatch,* Maitland †); in order to diminish the risk of this, Maitland urges that when a fruitless puncture has been made, a second puncture in another direction should not be made while the end of the trocar is still in the liver, since this manœuvre tends to enlarge the orifice and so favours hæmorrhage; if necessary, an entirely fresh puncture should be made. Cantlie,‡ who is a strong advocate of the use of the aspirating syringe, considers that the inferior vena cava is the only vessel likely to be wounded, and that if the needle is not introduced for more than 3½ inches, this danger can be eliminated. The risk from hæmorrhage is said to be greatest in those cases where there is no abscess. Further, a puncture may lead to peritonitis or may be the means of spreading infection in the liver by passing through the abscess and carrying the pus into other parts of the organ.

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[*] Rogers, L.: Brit. Med. Journ., 1903, vol. i, p. 1316.

[†] Godlee, R. J.: Medico-chirurg. Trans., vol. lxxxv, p. 121.

[‡] Godlee: Medico-chirurg. Trans., vol. lxxxv, p. 123.

[§] Boinet: Soc. de biolog. Paris, Dec. 29, 1900.

[‖] Osler: Medical News (N. Y.), April 12, 1902, p. 673.

DIFFERENTIAL DIAGNOSIS.

Suppurating Hydatid; Subdiaphragmatic Abscess; Pylephlebitis and Multiple Abscess; Suppurative Cholangitis; Intermittent Hepatic Fever; Pancreatic Cyst, Acute Pancreatitis; Suppuration in Rectus Muscle; Acute Hepatitis; Typhoid Fever; Malaria; New-growth; Lymphadenoma; Gumma; Ascites; Dilated Gall-bladder; Pleural Effusion and Empyema on Right Side; Tuberculosis.

Suppurating Hydatid Cysts.—In simple hydatid disease the liver is enlarged but the general health and nutrition are good, there is no fever, and there is a general absence of symptoms, such as pain, which form a striking contrast to the prominent local physical signs. No difficulty is therefore likely to arise in distinguishing between an ordinary hydatid cyst and abscess of the liver. When, however, a hydatid cyst becomes infected and suppurates, a condition of affairs exactly the same as abscess is brought about. In such cases the history that there had been a quiescent tumor in the position of the liver for a considerable time before the development of symptoms would suggest the exact state of affairs; otherwise it will be impossible to make an absolutely accurate diagnosis until the suppurating cyst is operated upon and its contents examined. Difficulty might conceivably arise in distinguishing between a simple hydatid complicated by fever, such as typhoid, and abscess of the liver.

Subphrenic Abscess.—A subphrenic abscess may be due to various causes, such as leakage of an hepatic abscess or suppurating hydatid cyst, suppurative cholecystitis, perforation of a gastric or duodenal ulcer, appendicitis, calculous or tuberculous disease of the kidney, and in rare cases from suppuration in the spleen or in connexion with malignant disease of the large intestine. In cases where an abscess, either tropical or one of the multiple abscesses seen in suppurative pylephlebitis or cholangitis, leaks on to the convexity of the liver and gives rise to a localized abscess between the diaphragm and the liver, the condition of affairs is for all practical purposes much the same as the original intrahepatic disease. When a localized peritoneal abscess is due to perforation of a gastric or duodenal ulcer, the cavity contains air and is often termed a subphrenic pyopneumothorax. The physical signs—resonance on percussion, a bell note, and succussion—distinguish it from hepatic abscess, which it does not so much resemble as a real pneumothorax. When a subphrenic abscess does not contain gas, it may be extremely difficult to differentiate it from an abscess in the liver. Thus in cases of neglected appendicitis a large abscess may pass upwards from the right iliac fossa, displace the right lobe of the liver forwards, and give rise to increase in the hepatic dulness and to apparent enlargement of the liver. It should be differentiated from a hepatic abscess by the history, the signs of appendicular mischief in the right iliac fossa, and by its tendency to bulge more into the right loin. The history or evidence of recent appendicitis are of some importance, for subphrenic abscess is commoner than hepatic abscess as a result of appendicitis. (Elsberg.*)

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* Hatch: Indian Med. Gaz., April, 1898.
† Maitland: Brit. Med. Journ., 1902, vol. i, 458.
‡ Cantlie, J.: Brit. Med. Journ., 1903, vol. ii, p. 656.

Suppurative Pylephlebitis or Multiple Abscesses.—The general resemblance of single and of multiple abscesses is often very marked, and an absolute diagnosis between them is not always justified. The points on which a distinction can be based are (i) local signs of abscess, such as fluctuation over a prominent swelling, or œdema of the body wall over the liver; (ii) the history of dysentery in the case of single abscess, or of appendicitis in multiple pylephlebitic abscesses. It must be remembered, however, that dysentery may be followed by multiple abscesses. This was seen in the dysentery affecting the British troops in the Boer War of 1899–1902. In a patient who has had dysentery, agglutination of the Shiga-Flexner bacillus would point to bacillary dysentery and to the intra-hepatic suppuration being multiple rather than single.

In the following case, seen on March 22, 1903, at Coltishall with Dr. Burton Fanning, multiple abscesses, secondary to appendicitis, very closely resembled a single abscess. A man aged forty-eight was seized seven weeks before with pain at the umbilicus which had continued ever since. There were dulness, friction, and distant bronchial breathing at the right base, but no enlargement of the liver in front. His temperature had fallen that morning to 96.4°, he was collapsed, looked almost moribund, and had a pulse of 140. Mr. H. A. Ballance did a transpleural operation, letting out serous fluid from the pleura, and opened an abscess about the size of a teacup in the back of the right lobe of the liver; no other abscesses could be seen. The man seemed much better and the temperature remained below normal for four days; it then became hectic and he died on April 2d. Dr. Burton Fanning did a postmortem examination and found the vermiform appendix gangrenous and the right lobe of the liver riddled with multiple abscesses. There was a good deal of serous fluid in the right pleural cavity.

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* Elsberg: Subphrenic Abscess after Appendicitis. Annals of Surgery, vol. xxxiv, p. 729, 1901.

Intermittent Hepatic Fever.—In intermittent hepatic fever depending on infective cholangitis due to calculi in the ducts periodical attacks of fever, jaundice, pain, and hepatic enlargement occur. The history in such cases would probably point to cholelithiasis, while the variation in the size of the liver or absence of enlargement, and the intervals of fair health, would tend to eliminate hepatic abscess. It is, however, well to bear in mind that infective cholangitis may go on to suppuration and that the temperature is then continuously raised.

Pancreatic Cyst.—A pancreatic cyst lifting up the left, or less often the right, lobe of the liver may imitate an abscess in the substance of that viscus. A pancreatic cyst is not accompanied by fever and often appears after a blow. But in very exceptional instances an abscess in the liver is not accompanied by pyrexia and may of course supervene after traumatism. As a rule, a pancreatic cyst forms a definite tumor in the left hypochondrium of large size and does not imitate an abscess even in the left lobe of the liver.

Acute pancreatitis with the production of an abscess limited to the cavity of the lesser sac of the peritoneum may, as shown in the following case, resemble an abscess in the left lobe of the liver.

A man aged forty came into St. George's Hospital on September 15, 1899, having been ill sixteen days, with a fluctuating tumor in the epigastrium which had been noticed four days before. It was in the position of the left lobe, but the rest of the liver showed no enlargement and the patient had never been out of England. A tentative diagnosis of suppurating hydatid cyst or of a pancreatic cyst was made. Mr. G. R. Turner operated the same day and opened a large abscess which was not in the liver but occupied the sac of the lesser omentum and went back to the spine. The patient did well for a time, but in October fever returned, he had rigors, and eventually died on November 8th. At the necropsy there was an abscess cavity in the lesser sac of the peritoneum with gangrene of the tail of the pancreas. There were suppurative pylephlebitis, multiple abscesses in the liver, and a left-sided empyema.

Suppuration in the Rectus Muscle.—Suppuration in the sheath of the rectus abdominis muscle is rare, and when it does occur, as it has been known to do after typhoid fever, is usually below the umbilicus. An abscess in the rectus muscle above the umbilicus might imitate a pointing hepatic abscess, but there is not complete dulness over the swelling and the liver is not enlarged. A needle introduced into an abscess in the abdominal wall remains stationary, while a needle projecting into an abscess in the liver should move with respiration. (Middeldorff's method.) This test may fail when the liver is firmly adherent to the abdominal wall (Osler *), and is not devoid of danger, since leakage may take place from the puncture in the liver.

A phantom tumor is likely to be mistaken for an abscess only when the patient has been in the tropics or has been exposed to dysentery. The gradual disappearance of a phantom tumor under a general anæsthetic is important in the diagnosis from hepatic abscess. Sir W. Bennett † has described, in a man who had had dysentery, a phantom tumor which was operated upon.

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* Osler: Practice of Medicine, p. 581, 4th ed., 1901.

† Bennett, W. H.: Lancet, 1902, vol. i, p. 3.

Since **acute hepatitis** precedes and may be considered an early stage of abscess, the question often arises whether suppuration has actually developed or not in a patient who has had dysentery and presents symptoms suggesting suppuration in the liver.

In a case of this kind operated upon by Bérard[*] on the assumption that there was an abscess, the patient was relieved considerably by the four punctures made into the liver.

In obscure forms of septicæmia the association of fever and enlargement of the liver from cloudy swelling may easily lead to a diagnosis of abscess. Remlinger[†] and Bozzolo have described a form of acute hepatitis as the infectious liver which imitates abscess very closely. In **typhoid fever** considerable hepatic enlargement sometimes occurs and may give rise to a diagnosis of hepatic abscess.[‡] This difficulty is more likely to arise in warm climates, where the two diseases are both prevalent.

The presence or absence of the agglutination reaction should be of very great assistance, but it might be present in a patient with hepatic abscess who had previously had enteric fever. An examination of the blood should always be made, since there is no leucocytosis in uncomplicated typhoid fever, while in abscess it may be present and be very considerable.

From **malaria** a diagnosis of hepatic abscess may be made by examination of the blood and a search for the parasite. In malarial cases treated with quinine the blood does not show the parasite; in such cases leucopenia points to malaria,[§] while in hepatic abscess there may be a high degree of leucocytosis. Cases of hepatic abscess with little enlargement of the liver may easily be regarded as malarial in the absence of a blood examination, while, conversely, chronic malaria with hepatitis may imitate hepatic abscess, in the enlargement, pain both in the liver and the right shoulder, and the general ill health. In malaria the hepatic enlargement is more uniform and is accompanied by enlargement of the spleen.

New-growth.—Confusion sometimes arises when rapidly growing malignant disease in the liver is associated with a raised temperature. A soft growth, especially when in the left lobe, may cause a bulging of the abdominal wall and give rise to a sense of fluctuation more or less obscure. In such cases, of which examples are given in the section on malignant disease of liver, exploration is the only sure method of coming to a diagnosis. It is very rare indeed for the converse to occur, viz., for an abscess to be regarded as a new-growth. It is more likely to occur in cases where the patient is extremely cachectic and deeply jaundiced.

In the following case of Osler's[‖] the condition was thought to be probably gall-stones with cancer. Summary: Woman, sixty-four years, dyspepsia for two years, loss of weight, pain in right side at intervals for three months, attacks of vomiting, slight jaundice, progressive weakness, no rigors, no leucocytosis, increase in size of liver, slight fever. Death. Amœbic abscess in right lobe of liver. No ulceration of intestines.

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[*] Bérard: Lyon Médical, May 8, 1902.

[†] Remlinger: La Presse Médicale, 1903, p. 86.

[‡] Bozzolo: Rivista Critica di Clinica Medica, March, 1902. H. Jones: Brit. Med. Journ., 1897, vol. ii, p. 1581.

[§] *Vide* L. Rogers: Brit. Med. Journ., 1902, vol. i, p. 831.

[‖] Osler: Medical News, April 12, 1902, p. 673.

Lymphadenoma.—In generalized lymphadenoma the temperature may closely resemble that of suppuration, and in rare instances there is very considerable enlargement of the liver.

Some years ago a man was under my care with a pedunculated mass in the left groin of many years' standing, which turned out to be lymphadenoma; he developed a hectic temperature and considerable enlargement of the liver. The condition was not unlike hepatic abscess and the question of operation was raised during life. He died at his home and a postmortem examination was performed by Mr. Archer of Vincent Square, who kindly sent me portions of the liver which showed lymphadenoma.

As a rule, there is not much enlargement of the liver in generalized lymphadenoma. In the blood examination of lymphadenoma there is usually no leucocytosis, while in abscess there may be a polymorphonuclear leucocytosis. Further, in lymphadenoma the superficial glands are usually affected.

Syphilitic Disease.—In some cases of syphilis there is continued fever and very considerable hepatic enlargement, and when this is met with in patients who have been in India or other countries where hepatic abscess is common, the resemblance to abscess is very likely to lead to a mistake. This is shown by the fact that cases of hepatic gummata have been operated upon under the idea that an abscess was present.

Ascites.—In a few cases an abscess has been so large as to imitate ascites, and the abdomen has been tapped on this assumption. This is more likely to occur in young subjects. Cases have been recorded by Hatch * and Powell.†

Dilated Gall-bladder.—Though it seems unlikely, a greatly dilated gall-bladder has been tapped under the idea that it was an hepatic abscess. There is a specimen (No. 1381) in St. Thomas' Hospital Museum illustrating this.

Right-sided Pleural Effusion.—There may be a very close resemblance between hepatic abscess and a right-sided pleural effusion. An abscess in the upper and back part of the right lobe of the liver will push the diaphragm up and give rise to dulness at the base of the lung. The dulness is said to be curved and to be higher in front and in the axilla than behind, but this is not always the case, as there may be a small concomitant pleural effusion in the right pleura due to the spread of inflammation through the diaphragm. The upward displacement of the diaphragm does not lead to displacement of the heart to the left in the same way that a large pleural effusion does, but this is not of much use, as an hepatic abscess rarely imitates a large pleural effusion. In a case of hepatic abscess the patient's general condition is worse than it would be in a comparatively small empyema or pleural effusion; further, the liver is usually enlarged downwards in abscess, while a pleural effusion of the size which an hepatic abscess imitates would not displace the liver downwards. As has been pointed out, hepatic abscess often gives rise to pleurisy and pleuritic pain, so that the question to be decided is whether there is an abscess in the liver or whether the whole disease is intrapleural. In a case of tropical abscess following typhoid fever (*vide* p. 125) the resemblance to an empyema was considerable.

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* Hatch: Indian Med. Gaz., Aug., 1898.

† Powell: Indian Med. Gaz., Feb., 1898.

Tuberculosis.—Cases of pulmonary tuberculosis with hectic temperature and with an enlarged fatty liver in which the physical signs of pulmonary disease are not prominent or have not been detected, have been diagnosed as hepatic abscess.* In hepatic abscess without any hepatic enlargement in patients who have never been out of England the continued temperature may, in the absence of any other signs, suggest generalized tuberculosis.

PROGNOSIS.

The prognosis of hepatic abscess, though always serious, and specially severe in the presence of complications, which will be referred to later, is by no means necessarily bad.

In a collection of 1094 cases the mortality was 30 per cent. (Solonoff †).

Lafleur ‡ considers the prognosis more unfavourable in amœbic than in other forms of hepatic abscess, but Manson § joins issue with him on this point. The prognosis is considerably modified by the period at which operative interference takes place. If the case is operated upon early, the outlook is favourable. Operation in private practice in India is, probably for this reason, much more successful than in hospital practice.

According to Moorhead, ‖ 75 per cent. of private cases and 50 per cent. of hospital cases recover. Hatch ** found that in some years 90 per cent. of the hospital cases terminated fatally, while in private practice the mortality was about 20 per cent.

When operative measures are only undertaken late, the prognosis is bad. Inasmuch as extensive destruction of the liver substance has taken place, the patient's strength is exhausted by the continued fever, and secondary results, such as pyæmia, have had time to develop.

Rupture of the abscess externally is favourable; rupture into the lung is generally regarded as fairly favourable, though convalescence may be tedious; thus, De Castro†† estimates that 75 per cent. recover, but Lafleur and Godlee take an unfavourable view of this complication. Rupture into the colon is usually followed by recovery. On the other hand, rupture into the general peritoneal cavity and into the pericardium are nearly always fatal. The presence of active dysentery is unfavourable. The existence of more than one abscess makes the prognosis bad; this is difficult to diagnose with certainty, but it should be suspected when the temperature remains raised in a case where an abscess has been opened and is discharging quite freely. When the abscess continues to discharge for a long time and signs of lardaceous disease—albuminuria, œdema of the feet, and diarrhœa—appear, the outlook becomes grave.

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* Josserand: Journ. de Méd., July 25, 1898.

† Solonoff: Brit. Med. Journ., 1903, vol. i, p. 262.

‡ Lafleur: Allbutt's System of Med., vol. iv, p. 168.

§ Manson, P.: Tropical Diseases, 1903, p. 457.

‖ Moorhead: Brit. Med. Journ., 1899, vol. i, p. 1032.

** Hatch: Lancet, 1902, vol. ii, p. 1543.

†† De Castro: Les Maladies du Foie dans les pays chaud, Paris, 1870.

After hepatic abscess and apparent recovery there is a danger of recurrence. Recurrence is more likely to occur if the patient remains in a tropical country or returns to it too soon after recovery. Marshall * advises that no patient should be allowed to return to a dangerous climate until two years have elapsed since the abscess was opened; and it is wiser that the patient should remain in England or a temperate climate permanently.

TREATMENT.

The treatment of hepatic abscess is essentially surgical and consists in removal of the pus and free drainage of the abscess cavity at the earliest opportunity. Medical treatment is only justifiable when there is doubt whether an abscess has formed, and during the period when acute hepatitis will explain the condition of affairs. During this period of uncertainty the medical treatment is the same as in acute hepatitis (*vide* p. 118). Probably before long it will be possible to treat this condition by the hypodermic injection of a bactericidal serum which is polyvalent and able to counteract the forms of micro-organisms most probably present, as shown by an investigation of the agglutinating properties of the patient's blood-serum.

In the stage when it is doubtful whether an abscess has actually formed and it is justifiable to hope that there is merely acute hepatitis, the patient should be kept in bed on a light diet. The bowels should be kept open, if necessary by mild laxatives, and local pain relieved by leeches, cupping, the application of an ice-bag, and other methods mentioned in the treatment of acute hepatitis. Chloride of ammonium in twenty-grain doses three times a day should be tried, but its value is somewhat problematical. Aspiration of the liver and removal of blood from the congested organ has been thought to be of use in preventing inflammation going on to suppuration, but, as already pointed out, it is not entirely free from risk. (*Vide* Acute Hepatitis.)

Aspiration.—Tapping the liver through the abdominal walls with a Dieulafoy's aspirator has been commonly advocated and is often successful. It is, however, dangerous, and should not be attempted. The abscess may leak into the general peritoneal cavity and set up general peritonitis; severe hæmorrhage may occur if the aspirator wounds a large branch of the hepatic artery, or possibly the aspirator may perforate one of the hollow abdominal viscera, such as the stomach or intestines.

In England Manson and Cantlie † have enthusiastically advocated drainage of the abscess by means of a trocar and cannula, and establishing a syphon drainage. This method has not found favour with Indian surgeons, who have had the greatest experience in the treatment of hepatic abscess. It is urged that this method is faulty in that it does not provide thorough drainage, that if the tube becomes displaced there is great difficulty in replacing it, and that if the tube gets out the pus may escape into the peritoneal cavity. After an abscess has been emptied by the cannula the liver may become so much smaller and altered in position that the cannula cannot be introduced into the abscess and drainage is prevented, while leakage may take place into the peritoneal cavity.

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* Marshall: Brit. Med. Journ., 1899, vol. i, p. 1387.

† Cantlie, J.: Brit. Med. Journ., 1903, vol. ii, p. 656.

The most satisfactory treatment of an abscess is free opening and drainage. The surgical procedure I cannot attempt to deal with, and the reader should refer to surgical text-books or to special works, such as Waring's "Surgical Diseases of the Liver." The position of the abscess must be first determined, and though it is not a harmless procedure, this must often be done by exploration with an aspirator under an anæsthetic. The abscess should be freely opened so as to allow of its interior being explored and any adjacent abscess opened. It is essential that adequate provision for free drainage should be made.

In cases where an abscess bursts into the lung, pleura, or peritoneum operation should be undertaken, and in the case of the peritoneum of course without any delay. (*Vide* p. 144.) In rupture into the colon no operation is necessary unless there are signs of peritonitis. Operative interference should be undertaken in the rare cases where rupture occurs into the pericardium or pelvis of the kidney, but in the former event death may be very rapid.

During convalescence from hepatic abscess tonics, fresh air, and nourishing food are necessary. Change of air to the seaside should be recommended, and if possible, the patient should not return to a tropical climate, and in any case not until two years have elapsed.

MULTIPLE ABSCESS IN THE LIVER.

The infection leading to multiple abscesses in the liver may reach the organ in several ways. The method of production provides a means of classifying multiple hepatic abscess.

(1) Ordinary pyæmic abscesses, in which the infection arrives by the hepatic artery.

(2) Abscess due to portal vein infection.
   (*a*) Multiple abscesses in bacillary and amœbic dysentery, in appendicitis, etc., due to infective emboli.
   (*b*) Suppurative pylephlebitis. (*Vide* p. 67.)

(3) Suppuration in and spreading from the bile-ducts. This is described under "Suppurative Cholangitis," and includes verminous abscesses due to worms which have travelled up the common bile-duct.

(4) Secondary abscesses due to the spread of infection from a large single abscess.

PYÆMIC ABSCESSES.

In general pyæmia numerous minute abscesses may be found in the liver.

In 24 cases of general pyæmia that were examined in the postmortem room of St. George's Hospital, 1890–1896, abscesses were found in the liver in 4 cases, multiple in 3, while in 1 there were two abscesses.

In infective endocarditis secondary abscesses in the liver are rare; thus, in 65 fatal cases of infective endocarditis collected by Kelynack* there was only one case in which the liver was affected.

An hepatic abscess may be secondary to suppuration anywhere in the body, even when there is no generalized pyæmia. In such cases the liver is probably in a state of diminished resistance, so that micro-organisms which would be destroyed elsewhere are able to flourish there. Percival Pott long ago stated that multiple abscesses in the liver were especially apt to follow injuries and suppuration in the head.

At the present time, when pyæmia is a comparatively infrequent disease, its commonest causes are acute infective periostitis and middle-ear disease. In cases of middle-ear disease multiple hepatic abscesses may be merely pyæmic. But it is noticeable that sometimes abscesses are not found in any other organ. This is difficult to explain. It might be said that the micro-organisms manage to get through the lungs without being arrested there and that the liver is the place of least resistance, the other organs in the body destroying the micro-organisms. Another though rather unlikely explanation is that the micro-organisms pass down from the head and drop, so to speak, through the right auricle into the hepatic veins. This passage of micro-organisms against the current of blood is termed retrograde embolism. It is rare, but it undoubtedly occurs.*

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* Kelynack: Encyclopædia Medica, vol. iv, p. 365.

It is a very speculative point, but it is possible that in the pre-anæsthetic days of Pott, retrograde infection of the liver from suppuration about the head was commoner than at the present time, when operations are quietly performed under an anæsthetic. Thus retrograde embolism is favoured by violent expiratory efforts which may result in blood, and the pus or micro-organisms in it, being driven out of the right auricle into the hepatic veins. Such expiratory efforts would be likely to occur at the time of any operation in the pre-anæsthetic days, and any pus or micro-organisms in the right auricle might thus be driven into the hepatic veins and infect the liver.

MULTIPLE ABSCESS IN CONNEXION WITH PORTAL VEIN INFECTION.

Multiple abscesses may occur as the result of widespread embolism of the intra-hepatic branches of the portal vein. Where this occurs without any pylephlebitis of the extra-hepatic parts of the portal vein, the process in the liver may be regarded as due to "portal pyæmia." In reality no hard-and-fast line can be drawn between such cases and typical pylephlebitis with multiple foci of suppuration in the liver.

Multiple abscess may occur in dysentery. It is rare in the form described as amœbic, rather less so in non-amœbic, dysentery. In both these forms of dysentery there may be a number of small abscesses all of about the same size and due to multiple embolism of the intra-hepatic branches of the portal vein. There may be a single large abscess which has, by infection of the branches of the portal vein, given rise to secondary and multiple foci of suppuration.

In amœbic dysentery the contents of the small multiple abscesses are barely liquid. The walls are formed of necrotic liver tissue and the abscesses have evidently originated in a portal space. There is usually absence of the ordinary small-cell infiltration seen in other forms of suppuration. (Lafleur.†) According to Rogers,‡ the small multiple abscesses are due to a mixed infection of amœbæ and pyogenetic cocci, while the large abscesses are solely due to amœbæ. Rogers figures small-cell infiltration in the small multiple abscesses. Multiple abscesses containing amœbæ have been found in cases where the intestines appeared normal. (Buxton.§)

In non-amœbic dysentery the multiple abscesses are like those seen in pylephlebitis. In the non-amœbic dysentery seen in South Africa in the War of 1899–1902 hepatic suppuration, when it occurred, was in the form of multiple liver abscesses without any evidence of pylephlebitis.

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* For a number of examples *vide* Welch: Allbutt's System of Medicine, vol. vi, p. 233.

† Lafleur: Allbutt's System, vol. iv, p. 158.

‡ Rogers, L.: Brit. Med. Journ., 1903, vol. i, p. 1317.

§ Buxton: Proc. Philadelphia Path. Soc., Jan., 1899.

Multiple abscesses from portal vein infection are most commonly secondary to appendicitis. The hepatic abscesses may be due to multiple emboli of pus-cells and micro-organisms which have passed up from a small abscess in connexion with the appendix, the intervening part of the portal and superior mesenteric veins being normal; or there may be suppurative pylephlebitis with multiple abscesses in the liver. In some instances there is a large abscess with smaller ones around it; the large abscess may be due to smaller and originally separate abscesses running together. From leakage or rupture of a small abscess general or localized peritonitis will result; in the latter case there may be an abscess between the convex surface of the liver and the diaphragm. Either an empyema on the right side or merely pleurisy with effusion is a frequent complication. Luckily hepatic suppuration is not a common complication of appendicitis; it is more likely to occur with a small abscess under considerable tension.

In 112 cases of appendicitis examined after death there were 2 cases of abscess of liver, 2 cases of suppurative hepatitis, and 2 of perihepatitis. (Langheld.*)

The following is a good example of what Dieulafoy calls the "appendicular liver":

A woman aged twenty-four with a history of appendicitis presented signs of a local abscess in the right iliac fossa; the appendix, which was thickened, and an ounce of pus in its neighbourhood were removed. The patient went on well for a week, when the discharge from the wound became very profuse; exploration showed that there was a suppurating cavity lined by coils of intestines. Her condition became one of chronic pyæmia, and in the last seven weeks of life the temperature was only normal on four occasions. At the autopsy the right lobe was riddled with abscesses; there was no general pylephlebitis or thrombosis of the portal vein, but a few intra-hepatic branches of the portal vein in the right lobe were thrombosed.

Sometimes the existence of the primary source of infection in the appendix is entirely latent and the patient comes under observation with a hectic temperature, rigors, and an enlarged liver.

Infection of the liver with the production of multiple abscesses is very seldom secondary to gastric ulceration. Murchison † recorded two cases of this kind. It is noticeable that suppurative pylephlebitis is also extremely rare after gastric ulcer. As a curiosity Lambert's ‡ case, in which a pin passed from the stomach into the right lobe of the liver and set up multiple abscesses, may be mentioned. In very rare instances multiple abscesses occur in the liver after typhoid fever; Gibbon § has collected nine examples. They may be secondary to intercurrent appendicitis and pylephlebitis, as in a case of Osler's,‖ due to embolism of the small branches of the portal vein, or to infection through the hepatic artery and secondary to an abscess elsewhere in the body.

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* Langheld: Quoted by Loison, Rev. de Chirurg., 1900, p. 522.

† Murchison: Trans. Path. Soc., vol. xvii, p. 145.

‡ Lambert: New York Med. Journ., Feb. 5, 1898.

§ Gibbon, J. H.: American Journ. Med. Sciences, vol. cxxv, p. 592.

‖ Osler: Trans. Associat. American Physicians, vol. xii, p. 380.

In a case of primary ulceration of the lower part of the rectum multiple abscesses in the liver, containing the Bacillus influenzæ similis, were found by Ophüls.* There was no septic thrombosis in the hæmorrhoidal or portal veins.

Suppuration in the pelvis may give rise to multiple abscesses in the liver, infection of the portal vein having occurred by means of the communications between the superior hæmorrhoidal branch of the inferior mesenteric vein and the branches (middle and inferior hæmorrhoidal) of the internal iliac veins.

Thus a prostatic abscess (Lancereaux †), gonorrhœal salpingitis (Handford ‡), perimetric abscess (Roughton §), and a suppurating submucous fibromyoma (Delestre ‖) have been known to give rise to multiple abscesses in the liver.

SECONDARY ABSCESSES DUE TO THE SPREAD OF INFECTION FROM A LARGE SINGLE ABSCESS.

A number of small abscesses are often found associated with a large single abscess cavity. In some instances the large abscess is due to a number of small abscesses becoming confluent. In other instances the small abscesses are secondary to infection from the originally single abscess, and are usually found in its neighbourhood. They are described by Davidson ** under the name of "secondary pyo-septicæmic abscess."

The clinical features, diagnosis, and prognosis in cases with the larger multiple abscesses in the liver are practically the same as in suppurative pylephlebitis, to which the reader should refer. The miliary abscesses in the liver in general pyæmia do not give rise to any special symptoms.

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* Ophüls: American Journ. Med. Sciences, vol. cxxii, p. 797, 1901.
† Lancereaux: Traité des Maladies du Foie et des Pancreas, p. 231.
‡ Handford: Trans. Path. Soc., vol. xxxvii, p. 267.
§ Roughton: St. Bartholomew's Hosp. Reports, vol. xxi, p. 173.
‖ Delestre: Bull. Soc. Anat., Paris, 1898, p. 219.
** Davidson: Allbutt's System of Med., vol. iv, p. 133.

PERIHEPATITIS.

Perihepatitis, or inflammation of the peritoneal capsule of the liver, may be acute or chronic.

ACUTE PERIHEPATITIS.

Causation.—In temperate climates acute inflammation of the peritoneum covering the liver and the underlying capsule is not a primary and independent condition, in the same way that pericarditis and pleurisy often are, but is secondary to disease in the liver or in the neighbourhood, and is usually quite subordinate to the primary affection. The only exception to this is the occurrence of traumatic perihepatitis such as follows fracture of the ribs on the right side; in such cases acute inflammation of the peritoneum covering the bruised or wounded areas of the liver may be found if there is a fatal termination. It has been thought (Cantlie *) that in the tropics, where acute perihepatitis is much commoner than in this country, it may be a primary affection like acute pleurisy; but it is reasonable to believe that its frequency in hot climates depends on the fact that active congestion of the liver and acute hepatitis, which are common, often extend to the surface of the liver and thus set up perihepatitis.

Acute perihepatitis may be secondary to acute hepatitis, suppuration inside the liver, such as abscess, suppurating hydatid cyst, pylephlebitis, and cholangitis. It may also be seen over rapidly growing nodules of new-growth involving the surface of the liver.

Acute inflammation of the peritoneal surface of the liver necessarily occurs in general peritonitis and in some forms of localized peritonitis due to inflammation, ulceration, and perforation of adjacent viscera; for example, in pancreatitis and inflammation localized to the lesser sac of the peritoneum, in cholecystitis, and in subphrenic abscess and subphrenic pyopneumothorax due to perforation of a gastric or duodenal ulcer, to appendicitis, or other causes. In such conditions where the surface of the liver happens to form the wall of an abscess cavity there is really no need to speak of pyoperihepatitis or pyopneumo-perihepatitis.† The first symptoms of a subphrenic abscess due to appendicitis may be those of acute perihepatitis.

In acute pleurisy, pneumonia, and pericarditis, inflammation may spread through the diaphragm and set up local peritonitis over the convexity of the liver. Occasionally it develops in the course of chronic venous engorgement of the liver, either as part of a passing, or of a terminal, infection of the liver. Acute perihepatitis is more often partial than universal.

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* Cantlie, J.: Encyclopædia Medica, vol. vii, p. 2.

† *Vide* Chauffard, in Traité de Médecine (Bouchard-Brissaud), tome v, p. 154, 1902.

Morbid Anatomy.—The surface of the liver in the affected area shows the dulling, loss of gloss, and slight granular appearance seen in acute peritonitis elsewhere. The vessels of the capsule are injected with blood and the parenchyma of the liver immediately under the capsule may show cloudy swelling.

At a later date organization of the fibrinous lymph takes place and filamentous adhesions are left as a memorial of past acute peritoneal inflammation, uniting the liver to the diaphragm, abdominal wall, and the adjacent viscera. These adhesions are not progressive and must not be considered as evidence of chronic perihepatitis. Such adhesions are very commonly found in the postmortem room, and in the great majority of instances have given rise to no symptoms during life. Exceptionally they may, however, induce pain and a sense of dragging in the right hypochondrium. If the adhesions involve the stomach, its movements may be so interfered with that dyspepsia of a very obstinate nature (adhesion dyspepsia) may be produced.

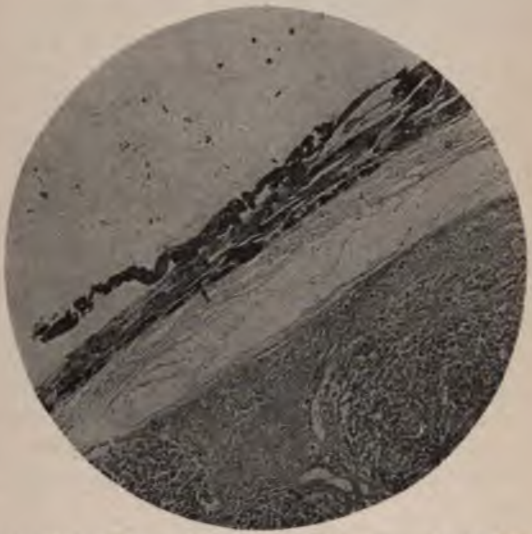

FIG. 22.—LYMPH IN ACUTE PERIHEPATITIS ON THE SURFACE OF A CIRRHOTIC LIVER WHICH SHOWS SOME LITTLE THICKENING OF THE CAPSULE.

The lymph appears opaque. Some separation has taken place between the layers of the thickened capsule. (Photomicrograph by S. G. Penny, Esq.)

Mr. Allingham performed laparotomy on a patient with very severe dyspepsia, under the care of Dr. Vernon Jones, and found firm adhesions between the stomach and liver; these were divided and the symptoms were relieved. There was a history of acute perihepatitis twelve years before in India.

As an example of perihepatitis due in all probability to a terminal infection the following case is of interest:

A boy aged ten years died in St. George's Hospital with adherent pericardium, a dilated and hypertrophied left ventricle, and signs of backward pressure. In the last few days of life he had pain over the liver and a raised temperature, but no jaundice. At the autopsy there was recent lymph on the surface of the liver, which weighed 29 ounces. On section the liver was swollen, of a mottled yellow colour, not nutmeggy. Unfortunately none of the liver was preserved for more minute examination, but its description suggests that a terminal infection had fallen on the liver and given rise to acute inflammation of its capsule and degenerative changes in the liver cells.

Signs and Symptoms.—There is pain over the liver, which is made worse on respiration and is accompanied by a friction rub. The right side of the chest moves little and the liver is tender to the touch, and when an attempt to examine it is made, the overlying abdominal muscles at once become rigid. If the liver is grasped between the two hands, placed in front and behind, and moved backwards and forwards, acute pain is elicited, which may run up to an area between the clavicle and the acromion process of the scapula on the front of the chest (Cantlie), thus differing from the shoulder pain of intra-hepatic disease. Dry cough may occur and be readily induced by examination of the liver. Fever, sense of weight in the hypochondrium, and other symptoms may be due to accompanying and underlying hepatitis and active congestion. Local acute perihepatitis may give rise to some ascites, but very rarely to a sufficient amount to be detected clinically. I am convinced that slight ascites may be thus produced from observation during laparotomy on a case of pylephlebitis with local involvement of the capsule of the liver.

Diagnosis.—It must be remembered that perihepatitis is practically always due to some underlying condition, and that diligent search must always be made for the primary disease, such as abscess and other forms of intra-hepatic suppuration, hepatitis, new-growth, chronic venous engorgement, etc. Acute perihepatitis is very likely to be confused with acute pleurisy on the right side; indeed, in many cases the two conditions may co-exist, the inflammation spreading from one serous surface to the other. In differentiating these two conditions Cantlie lays stress on grasping the liver between the hands and moving it; the pain running up into the supraclavicular fossa is regarded as diagnostic of perihepatitis.

Treatment.—Rest and warmth in bed are important, while the underlying cause is sought for and treated. Treatment of the inflamed capsule of the liver will consist chiefly in the relief of pain. If severe, half a dozen leeches may be applied and be followed by a poultice; in slighter cases hot fomentations over the liver, or counterirritation in the form of a mustard poultice or leaf, will be sufficient. Dry cupping often gives considerable relief. Strapping the side, as in the method employed for fractured ribs, will minimize movement and pain. A light milk diet should be given at first until the patient feels able to take solid food.

CHRONIC PERIHEPATITIS.

Under this heading two conditions of very different importance are included—(i) local and (ii) universal perihepatitis.

LOCAL CHRONIC PERIHEPATITIS.

This condition may be due to a number of different causes. In its slighter degrees it is seen as the result of pressure in tight-laced livers, when a belt has been worn, or may result from the communicated pulsations of a large heart. The thickening of the capsule, often associated with some atrophy of the liver substance immediately subjacent, is analogous to the milk spots so commonly seen on the surface of the heart. In many cases this local thickening of the capsule is associated with backward pressure due to obstructive heart or lung disease; in such cases the distension, and perhaps pulsation, of the liver, by giving rise to increased friction and attrition, helps to call forth the capsulitis. In 18 cases of Hale White's * backward pressure was present in 10. In 87 cases of tricuspid stenosis recorded by Pitt † perihepatitis was present in 11. The local perihepatitis is occasionally part of cancerous or tuberculous peritonitis, or may be found over a gumma or hydatid cyst embedded in the liver; it may also be due to the irritation of a calculous gall-bladder or to a gastric ulcer. Capsulitis of the spleen is frequently associated with it (in 9 out of 18 of Hale White's cases).

Local perihepatitis very seldom goes on, so far as is known, to the diffuse or universal form. Nicholls ‡ records a case of local perihepatitis due to cholecystitis in which this transformation was in progress. The thickened portion of the capsule of the liver does not peel off, but is firmly adherent; it thus contrasts with the "false membranes" seen in universal perihepatitis, which lie on the surface of and not in the substance of the capsule of the liver. The local thickenings on the liver resemble anatomically the milk spots on the heart and the corneal fibromata on the capsule of the spleen. Microscopically they show parallel strands of well-formed fibrous tissue with cells between them, but do not contain blood-vessels. The fibrous tissue shows hyaline change. These local areas of chronic capsulitis may be adherent to adjacent parts, but usually they are free.

Local chronic perihepatitis may account for some pain and tenderness over the liver and may possibly give rise to a friction rub over the organ. Strictly localized perihepatitis does not give rise to ascites; but in some cases where areas of chronic perihepatitis are scattered over the surface of the liver so as to give rise to a transition between local and universal chronic perihepatitis, ascites may possibly be due to this cause. The cases of ascites in cirrhosis of the liver which are frequently tapped may be due to this form of chronic peritonitis. Strictly localized chronic perihepatitis is of little or no clinical importance apart from the associated morbid conditions of the liver.

Treatment.—If the condition is suspected and there is pain, it may be treated by local applications, such as poultices, hot compresses, or belladonna plasters, but usually no special treatment is required.

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* Hale White: Trans. Clin. Soc., vol. xxi, p. 219. Allbutt's System of Medicine, vol. iv, p. 118.

† Pitt: Allbutt's System, vol. vi, p. 23.

‡ Nicholls, A. G.: Studies from the Royal Victoria Hospital, Montreal, vol. i, No. 3, p. 41, 1902.

UNIVERSAL CHRONIC PERIHEPATITIS.

Synonyms: Diffuse Chronic Hyperplastic Perihepatitis, Chronic Hyaline Perihepatitis, Chronic Deforming Perihepatitis, Icing Liver (Zuckergussleber).

History, etc.—The condition was observed by Budd[*] in 1852. Curschmann[†] in 1884 described the morbid changes in detail and invented the graphic name of sugar-iced liver (Zuckergussleber). The writings of Hilton Fagge[‡] and Hale White[§] of Guy's Hospital have been of great value in distinguishing the clinical aspects of perihepatitis from those of cirrhosis, and in drawing attention to the relationship between chronic interstitial nephritis and chronic perihepatitis. Nicholls[‖] of Montreal has recently (1902) published a monograph of 80 pages, and Kelly[**] has written an exhaustive paper on this subject.

This condition has received a number of rather cumbrous names, but is usually only a local manifestation of diffuse chronic peritonitis. It is in fact artificial to separate chronic universal perihepatitis from diffuse chronic peritonitis. The chronic inflammatory change may begin in the peritoneal coat of the liver and subsequently involve the adjacent peritoneum, or it may extend to the serous covering of the organ in cases of more or less general chronic peritonitis. As a matter of fact, the name chronic perihepatitis suggests a more intimate relationship to the liver than actually exists. A more accurate though longer descriptive title would be chronic peritonitis with perihepatitis, or chronic peritonitis involving the liver.

Pathogeny.—The chronic peritonitis, of which chronic perihepatitis is part, is usually that form spoken of as simple, since it is not manifestly due to tuberculosis or to new-growth. It is characterized by a widespread fibrosis with cicatricial contraction, so that the mesentery and omentum are shortened and the viscera become inclosed in a firm casing which contracts upon and compresses them. In considering the question of causation, it will be convenient to divide cases of chronic perihepatitis and peritonitis into three groups:

(I) When associated with varying degrees of chronic inflammation of the pericardium and pleuræ (multiple serositis).

(II) When associated with arteriosclerosis and granular kidneys.

(III) When associated with other conditions.

I. *When Associated with Varying Degrees of Chronic Inflammation of the Pericardium and Pleuræ (Multiple Serositis).*—Chronic peritonitis and chronic universal perihepatitis may be associated with varying degrees of the same change in, or in connexion with, the serous membranes in the thorax—the pericardium and pleura. The combined changes in more than one serous membrane are spoken of as multiple serositis, polyorromenitis, or Concato's disease. There may be a descending scale in the extent of the associated intrathoracic changes. Thus, there may be extensive fibrosis of the mediastina with adherent pericardium and pleuræ (indurative mediastino-pericarditis), adherent pericardium with thickening and obliteration, partial or complete, of both or of only one pleura, or only a calcified and adherent or an adherent pericardium. In this class the inflammatory change is most intense on each side of the diaphragm, and fades off in the more distant parts of the peritoneum and pleuræ; probably the constant movement of the diaphragm assists in keeping up the morbid process when once it has been started. The inflammatory change beginning on one side of the diaphragm readily spreads through the lymphatics to the neighbouring serous membrane. In most of the cases the inflammatory change is primary in the pericardium or pleura and spreads to the convexity of the liver, but in some it is probable that it begins as an acute inflammation close to the convexity of the liver and subsequently becomes chronic and extends to the right pleura and pericardium. In chronic perihepatitis associated with intrathoracic changes of the same kind the kidneys are, as a rule, healthy, or merely show chronic venous engorgement. But in some instances they are granular and thus merge into the next group.

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[*] Budd: Diseases of Liver, p. 139.

[†] Curschmann: Deutsche med. Wochensch., 1884, S. 564.

[‡] Hilton Fagge: Principles and Practice of Med., vol. ii, p. 294.

[§] Hale White: Trans. Clin. Soc., vol. xxi, p. 219. Guy's Hosp. Reports, vol. xlix, p. 1.

[‖] Nicholls, A. G.: Studies from the Royal Victoria Hospital, Montreal, vol. i, No. 3, April, 1902.

[**] Kelly, A. O. J.: American Jour. Med. Sciences, vol. cxxv, p. 116, Jan., 1903.

A well-marked example of chronic proliferative peritonitis and périhepatitis associated with chronic indurative mediastino-pericarditis was seen in a man aged fifty-five years, an in-patient at St. George's Hospital in 1896. He presented ascites, which required tapping 26 times, and œdema of the legs; during life mediastinal growth appeared probable from the existence of post-sternal dulness. At the autopsy the pericardium was firmly adherent to the heart and to all the surrounding parts, especially to the region of the thymus gland, which was occupied by very dense firm fibrous tissue (microscopically only fibrosis). There were very dense pleural adhesions, ½ an inch thick on the left side, and universal chronic peritonitis and perihepatitis. The liver weighed 72 ounces and microscopically showed early cirrhosis, though to the naked eye it appeared normal. The kidneys weighed 8 ounces each and were healthy.

A number of cases of universal chronic perihepatitis associated with adherent pericardium have been recorded and the condition is not in reality rare.

Gilbert and Garnier[*] described 11 cases under the name of symphyse péricardio-périhépatique. Heidemann,[†] in a paper on the results of adherent pericardium, collected 7 fresh cases. Kelly,[‡] in his elaborate account of multiple serositis, referred to 27 cases of universal perihepatitis associated with adherent pericardium.

I have seen 2 cases in which chronic perihepatitis was associated with, and probably due to, extension of inflammation through the diaphragm, form an adherent pericardium that had undergone calcification.

A closely allied condition to universal chronic perihepatitis associated with adherent pericardium was described by Pick[§] as pericarditic pseudo-cirrhosis of the liver, in which, together with latent adherent pericardium, there was ascites due to fibrous hyperplasia and circulatory disturbance in the liver. Any evidences of chronic inflammation of the peritoneum were regarded by Pick as accidental or secondary to ascites and chronic venous engorgement. Cases of this kind without chronic universal perihepatitis or chronic peritonitis certainly occur, and have already been described as exaggerated cases of chronic venous engorgement of the liver. (*Vide* p. 97.) Kelly,[*] on the other hand, groups together under the heading of "multiple serositis" these cases of pericarditic pseudo-cirrhosis and the cases of "iced liver," or, as they are usually called in England, chronic universal perihepatitis, and while admitting some anatomical distinctions, regards them as very much alike clinically.

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[*] Gilbert and Garnier: Soc. de biolog., Jan. 15, 1893.

[†] Heidemann: Berlin. klin. Wochen., 1897.

[‡] Kelly, A. O. J.: American Journ. Med. Sciences. vol. cxxv, p. 116, 1903.

[§] Pick: Zeitschrift f. klin. Med., 1896, Bd. xxix, S. 385.

(II) *Chronic Perihepatitis Associated with Arteriosclerosis and Granular Kidneys.*—Chronic perihepatitis is frequently associated with arteriosclerosis and granular kidneys; this was so in 19 out of Hale White's [†] 22 cases. In this group there is not the same intimate relationship between chronic perihepatitis and thoracic lesions as in the previous category, though the two conditions may be found together.

There appears to be some connexion between arteriosclerosis and fibrosis of the serous membranes (perivisceritis).[‡] It is conceivable that arteriosclerotic change in the kidneys is a disposing cause of chronic inflammation in the body generally. As Flexner [§] has shown, the bactericidal power of the blood is reduced in chronic renal disease and so allows microbic infections to occur. It is reasonable to believe that chronic perihepatitis and peritonitis might be produced by micro-organisms of no great virulence but capable of inducing considerable fibrosis. It is more probable that the process is microbic than that it is purely toxic and due to an altered (uræmic) condition of the blood. In either case the influence of arteriosclerosis and granular kidneys should lead to a similar change in the other serous cavities, the pleura and pericardium. This condition of combined inflammation of several serous membranes—polyorromenitis[‖] or multiple serositis—does sometimes occur in cases of granular (arteriosclerotic) kidneys, but it is by no means constant to find another serous membrane involved as well as the peritoneum. In order to explain cases where the peritoneum alone is attacked or is much more affected than any of the other serous membranes, it may be suggested that the facilities for infection are greater in the abdomen and that the resistance of the peritoneum has been specially lowered in these cases. It has been thought that arteriosclerosis of the small vessels of the peritoneum may produce chronic peritonitis[**]—a fibrosis due to impaired nutrition.

As an example of this form the following case may be quoted: A woman aged sixty-nine years had ascites requiring paracentesis; eventually she died in an extremely thin and cachectic state. The autopsy revealed granular kidneys, universal chronic peritonitis, a liver which weighed only 23 ounces, and on section looked cirrhotic, but not in the least nutmeggy. Microscopically the liver was typically nutmeggy and only showed slight replacement fibrosis. The heart weighed 8 ounces, and was devoid of epicardial fat; on section it showed brown atrophy of the myocardium.

A well-marked example of chronic universal perihepatitis with similar changes in the pleura and pericardium, and granular kidneys occurred in a woman who died in St. George's Hospital in coma in 1898. She had often been treated for myxœdema. She had ascites, universal chronic perihepatitis, perisplenitis, and peritonitis with a number of fibrous nodules in the peritoneum near the umbilicus (peritonitis fibrosa). Both layers of the pericardium were much thickened, and the cavity contained excess of fluid. The pleuræ were both thickened, showed adhesions, and contained about 8 ounces each of clear fluid. The liver (60 ounces) was nutmeggy and free from cirrhosis. Microscopically there was a dense layer of fibrous tissue on the surface of the liver replacing the capsule. There was subcapsular atrophy of the liver cells, while the branches of the hepatic artery and portal vein appeared as prominent objects from a very peculiar swelling of their coats. (*Vide* Fig. 23.) This change seemed to be due to myxomatous degeneration and to be connected with the primary disease—myxœdema. The kidneys (right, 3½ ounces; left, 3½ ounces) were red and granular. The heart weighed 14 ounces.

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[*] Kelly, A. O. J.: American Jour. Med. Sciences, vol. cxxv, p. 116, Jan., 1903.

[†] Hale White: Trans. Clin. Soc., vol. xxi, p. 221.

[‡] Labadie, Lagrave et Deguy: Archiv. Général. de Méd., 1898, p. 411 (Perivisceritis).

[§] Flexner: Journ. Experimental Medicine, vol. i, 1896.

[‖] For an account of this condition see Taylor, F.: Brit. Med. Journ., 1900, vol. ii, p. 1698; Kelly, A. O. J.: American Journ. of the Medical Sciences, vol. cxxv, p. 116, 1903.

[**] Delpeuch: Archives Générales de Médecine, 1884. Quoted by Labadie, Lagrave and Deguy: Archives Générales de Médecine, 1898, p. 411.

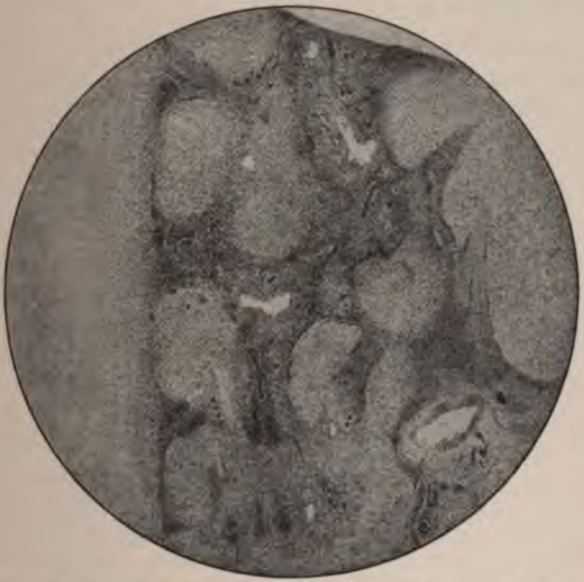

FIG. 23.—MICROSCOPIC SECTION SHOWING HOMOGENEOUS HYALINE MEMBRANE ON THE SURFACE OF THE LIVER WITH A SIMILAR HYALINE CHANGE IN THE FIBROUS TISSUE OF THE PORTAL SPACES IN THE UNDERLYING LIVER SUBSTANCE. FROM A CASE OF MYXŒDEMA.

The thymus gland could not be found, and the pituitary body was not enlarged. The thyroid gland was very atrophied and of a pale yellow colour. There was some obsolete tubercle in the lungs.

(III) *Universal Chronic Perihepatitis Due to Other or Obscure Causes.*—In a few instances perihepatitis may be associated with syphilitic lesions of the liver, but, as a rule, hepatic gummata only give rise to a local thickening of the capsule of the liver.

Cheadle * expresses his belief that perihepatitis is more marked and frequent in association with syphilitic disease of the liver than in any other condition. In 22 cases of universal perihepatitis collected by Hale White † there were 3 in which syphilis was the apparent factor. Numerous small syphilitic gummata may so extensively involve the capsule as to set up universal perihepatitis. (Sharkey,[*] N. Moore.[†])

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* Cheadle, W. B.: Some Cirrhoses of the Liver, 1900, pp. 41, 43.

† Hale White: Allbutt's System, vol. iv, p. 121.

In the following case universal perihepatitis and chronic peritonitis were associated with the presence of three old and several recent gummata in the liver. The patient, a man aged thirty-seven years, who denied syphilis, but drank 3 pints of beer daily, had been well until three and a half months before his death, when he began to suffer from morning sickness and abdominal pain. A month later he became jaundiced, ascitic, œdematous as to his legs, and vomited a little blood. He was tapped twice, 40 pints being removed. The urine was free from albumin. After death there was general chronic peritonitis of not very marked degree and universal chronic perihepatitis; the liver weighed 56 ounces and contained 3 gummata in the right lobe and several scars and recent gummata in the left lobe; there was no general fibrosis of the liver. There appeared to be kinking of the portal vein and bile-duct in the portal fissure, but on cutting away the adhesions around them the vein and duct were found to be unobstructed. The kidneys weighed 6 ounces each and were healthy and free from lardaceous change. The heart weighed 8 ounces and was healthy.

In rare instances universal chronic perihepatitis may be associated with intra-abdominal malignant disease or be due to tuberculosis. In the latter case the lesions are those of chronic fibrosis and are very different from those of ordinary tuberculous peritonitis.

Hale White expressed a very definite opinion that universal chronic perihepatitis was never due to tuberculous or malignant peritonitis. This is probably too dogmatic a statement. Nicholls after discussion of the available data concludes that some cases are undoubtedly due to tuberculosis.

Chronic peritonitis and perihepatitis may be associated with and possibly due to that rare condition—cirrhosis of the stomach—the fibrotic process extending from the stomach to the peritoneum. This association was well illustrated by the following case:

A man aged forty-eight was under my care in St. George's Hospital in November and December, 1899, with a well-marked alcoholic history and the facies of hepatic cirrhosis. He was tapped twice for the relief of ascites in those two months, and the question of operative interference, with the object of setting up artificial peritoneal adhesions, was being considered when he suddenly died. The autopsy showed dilatation of the left ventricle of the heart, perihepatitis, chronic peritonitis, extreme cirrhosis of the stomach, and hypertrophy of the muscular coat of the œsophagus. There was extreme thickening of the submucous coat of the stomach, but no trace microscopically of carcinoma. The substance of the liver was healthy, and the kidneys were normal. I have seen one other case of this kind. Most authorities, however, regard "cirrhosis of the stomach" as a diffuse carcinomatous infiltration.

It may also be found in cases of backward pressure without any adherent pericardium. In other instances alcoholism has been thought to be the only antecedent condition, while sometimes, as in the very extreme condition—systematic hypertrophic cirrhosis of the peritoneum described by Du Pacquier[‡]—no cause is forthcoming.

It is conceivable that in some instances chronic perihepatitis and peritonitis may start from foci of local irritation which usually only give rise to circumscribed perihepatitis. In such cases the widespread effect is analogous to the development of a keloid in the skin after a slight injury.

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[*] Sharkey, S. J.: Trans. Path. Soc., vol. xxxiv, p. 118.

[†] Moore, N.: idem, p. 133.

[‡] Du Pacquier: Archiv. Général. de Médecine, Dec., 1897.

Nicholls * recorded in full detail a case of widespread chronic hyperplastic inflammation of the serous membranes (including perihepatitis) in a woman aged forty-eight with a chronic duodenal ulcer and slight chronic interstitial nephritis. The changes in the serous membranes were referred to irritation and possibly infection from the duodenal ulcer.

Morbid Anatomy.—The surface of the liver is covered over by a crust or coating of fibrous tissue of cartilaginous consistence. It is glistening and white, resembles the icing of confectioners, and thus accounts for the name "sugar-iced liver" (Zuckergussleber) which has been applied to this condition by Curschmann. The surface of this casing is pitted or fenestrated, probably as a result of rupture during its spontaneous shrinking and contraction. This coat can be peeled off, leaving the peritoneal surface in a fairly healthy state. The liver is compressed and deformed by the constant traction which the cicatricial tissue exerts upon it. Thus the anterior margin may be bent upwards and over so as to touch the convex surface. The convexity of the liver is usually much more affected than the under surface, and of course the portions uncovered by peritoneum are free from the change. The gall-bladder is nearly always collapsed and buried under thick membrane and is with difficulty discovered, its position being sometimes merely indicated by a depression.

In the one case where I have seen it dilated there was malignant disease of the peritoneum in addition to chronic perihepatitis and peritonitis.

Even when the portal fissure is invaded by the perihepatitis the portal vein hardly ever becomes compressed as might be expected. Hale White † points out that if the portal vein were compressed or kinked the bile-duct would also be affected, and that this must be very rare from the clinical absence of jaundice. His point is that ascites is due to the chronic peritonitis and not to mechanical interference with the portal vein, for in two cases—very exceptional ones—where universal chronic perihepatitis existed without any chronic peritonitis there was no ascites. In the case given on page 168, however, there appeared to be kinking of the portal vein and bile-duct. There may be adhesions between the surface of the liver and the diaphragm, abdominal walls, and adjacent organs.

The liver is usually soft, fatty, and shows chronic venous engorgement with general atrophy. Multilobular cirrhosis is very rarely combined with well-marked perihepatitis of the kind now under discussion. It is true that adhesions and opacity with thickening of the capsule are often seen in advanced cirrhosis, but the combination of the "iced liver" and cirrhosis is so rare that in Nicholls' ‡ monograph only one example is admitted. Superficial fibrosis spreading in from the surface (Glissonian cirrhosis) is not uncommon, but it does not extend for any distance.

Microscopically the thickened membrane is seen to lie on Glisson's capsule, which is thrown into wavy folds. This "icing" membrane is composed of well-formed fibrous tissue arranged in horizontal laminæ with a few nuclei between them. The structure is like that of a lamellar fibroma of the spleen. The fibrous tissue has undergone hyaline degeneration. From the presence of this change Nicholls speaks of the condition as hyaloserositis. The membrane does not contain blood-vessels and there is usually a distinct line of separation between the membrane and the underlying capsule of the liver. In the deeper layers and between it and the underlying capsule, which is thrown into folds, there are collections of leucocytes and mast cells; there is no reaction for fibrin. (Nicholls.)

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* Nicholls, A. G.: Loc. cit.

† White, Hale: Allbutt's System of Medicine, vol. iv, p. 120.

‡ Nicholls: Studies from Royal Victoria Hospital, Montreal, vol. i, No. 3, p. 26.

The condition of the underlying liver varies a little; it is rarely absolutely normal, being generally atrophied, with fatty and pigmentary change in the liver cells, while chronic venous engorgement is very common. Not very rarely there is slight Glissonian cirrhosis or fibrosis spreading a short way into the substance of the liver. The underlying liver tissue may show a similar hyaline change in the fibrous septa. (Fig. 23.)

The spleen is usually rather larger than natural, and its capsule shares in the chronic thickening of the peritoneum. It is often firmly adherent to the diaphragm and abdominal wall.

The kidneys in cases associated with indurative mediastino-pericarditis, adherent pericardium, and chronic pleurisy may show little change except chronic venous engorgement. When chronic perihepatitis is associated with arteriosclerosis, the kidneys usually share in the change and are red and granular.

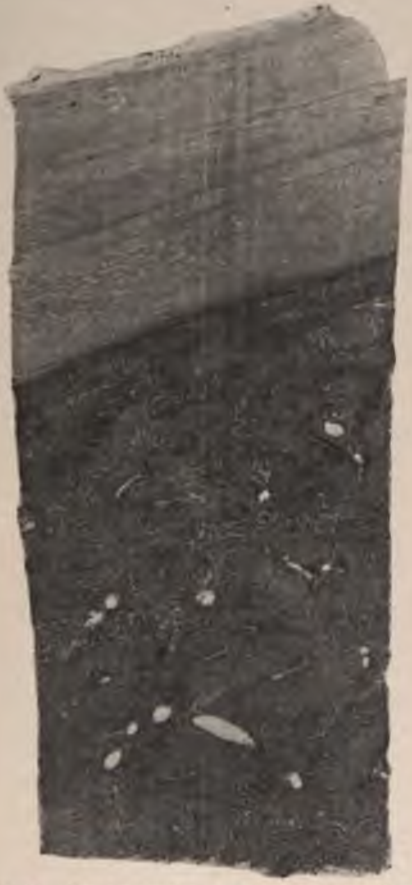

FIG. 24.—PHOTOMICROGRAPH SHOWING THE THICK "ICING" IN CHRONIC UNIVERSAL PERIHEPATITIS.

The line of distinction between it and the liver is well seen. The liver showed some fibrosis and chronic venous engorgement. (Photomicrograph by Dr. H. Spitta.)

The peritoneum shows the same fibroid and hyaline change as the capsule of the liver, and undergoes the same cicatricial contraction and puckering. The great omentum is rolled up and transformed into a hard cord, the mesentery is thickened, and by its retraction tethers the intestines, which are much shortened, to the spine, so that they cannot reach to the front of the abdominal wall. As a result of this the abdomen may be uniformly dull in front.

The right pleura is more often affected by the chronic fibroid change than the left. The body as a whole is thin and may be extensively œdematous.

Clinical Picture.—*Sex.*—The sexes are about equally affected, thus contrasting with cirrhosis, in which the male sex provides a large majority of the patients.

In Hale White's * 21 cases there were 13 males and 8 females. In 20 cases that I have tabulated the sexes were equally affected.

Age.—The age varies considerably, but is generally about the same as in cirrhosis.

In Hale White's cases the average age was forty-seven and a half years, the youngest being twenty-nine and the oldest sixty-nine years. In my 20 cases the average age was 42.6 years, being practically the same in the two sexes; the extremes were fourteen and sixty-nine years.

Heredity does not appear to have any influence in the development of the disease, in spite of the fact that arteriosclerosis, which appears to play some part in the production of chronic perihepatitis and chronic peritonitis, is to some extent hereditary.

Onset.—Usually the development of ascites is gradual, but in some instances is acute; this was so in 6 out of 14 cases selected by Nicholls. The condition has been thought to date back to, and be started by, an acute inflammatory change involving the pericardium or liver.

Course.—The course of the disease is slow and extends over years. Nicholls finds that the duration of the disease is from two to sixteen years. Ascites, which constantly recurs, is the main symptom, but the general health and strength are fairly maintained for a long time. Emaciation gradually appears and death occurs from some intercurrent disease or secondary infection, such as acute peritonitis, or pneumonia.

In one case under my care death was due to influenza, and at the autopsy there were two small recent ulcers in the first part of the duodenum with acute inflammation of the duodenum.

Signs and Symptoms.—The condition is practically always accompanied by ascites, and thus contrasts with cirrhosis, which may be quite latent. Ascites is the chief physical sign and requires frequent tapping. Thus, Osler † refers to a child in whom this operation was performed 121 times. As time goes on tapping becomes necessary at shorter intervals and may be called for every fortnight or even sooner. Ascites is compatible with fair health and strength during the earlier part of the disease, and in the intervals between the tappings the patient may be up and about.

A woman suffering from universal chronic perihepatitis, secondary to calcification of the pericardium, who eventually died after her sixtieth tapping, was married after being tapped twenty times. She was under the care of my colleague, Dr. Ewart, in St. George's Hospital.

The recurrence of ascites combined with fair health, or at any rate freedom from toxæmia, are important points in the diagnosis from cirrhosis. The ascitic fluid is clear and straw-colored, but contains a high percentage of albumin (3 per cent.), which allies it with inflammatory exudations rather than with passive transudations. If allowed to stand, threads of fibrin may be formed. Occasionally the ascites is encysted from the presence of adhesions. The liver may be enlarged and palpable in the earlier stages, but becomes smaller as time goes on. Ascitic distension of the abdomen may interfere with the estimation of the size of the liver and spleen. Some enlargement of the spleen is usual in young subjects.

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* Hale White: Allbutt's System of Medicine, vol. iv, p. 121.

† Osler: Practice of Medicine, p. 576, 4th ed., 1901.

The omentum may be felt as a transverse band passing across the abdomen, and must not be regarded as the lower border of the liver. The subcutaneous abdominal veins (superior and inferior epigastric veins) are sometimes enlarged and are seen to form a collateral circulation between the superior and inferior venæ cavæ. These veins do not converge towards the umbilicus, as is the case in the collateral circulation of portal obstruction. Jaundice is almost always absent; it was present in only one of the 22 cases analysed by Hale White, and when it occurs is probably due to some independent or concomitant factor. The *urine* is diminished in amount and may contain albumin, either from chronic venous engorgement or from arteriosclerotic change in the kidneys.

In addition to ascites there may be signs of the conditions specially associated with chronic perihepatitis: viz., (i) adherent pericardium, chronic mediastinitis, dense pleural adhesions, or (ii) arteriosclerosis and granular kidney. Œdema of the legs is often seen late in the disease and may extend to the trunk and upper extremities.

Since the liver substance is well preserved, there is little constitutional disturbance and no tendency to hepatic inadequacy or to hæmorrhages, drowsiness, and the other toxæmic manifestations seen in cirrhosis. If such symptoms do develop, they are to be referred to concomitant renal disease. It must be remembered that in many cases which clinically present themselves as failing heart from granular kidneys, with ascites and general dropsy, there is universal perihepatitis. There may be loss of appetite and dyspepsia, while, from the relaxed and flabby condition of the abdominal walls, constipation is often induced. Gastro-intestinal hæmorrhage does not occur unless there is some complication, such as gastric or duodenal ulcer or, in rare instances, cirrhosis.

Diagnosis.—The presence of long-continued ascites not manifestly due to obstructive heart or lung disease, or to chronic parenchymatous nephritis, points very strongly to universal chronic perihepatitis and peritonitis.

Differential Diagnosis.—*From Cirrhosis of the Liver.*—When ascites develops in cirrhosis the end is usually near and paracentesis is not likely to be often required unless the ascites is due to associated chronic peritonitis. Repeated tappings therefore are strongly in favour of chronic peritonitis and perihepatitis; evidence of arteriosclerotic kidney disease would also strengthen this view. Jaundice, grave constitutional and toxæmic symptoms, hæmatemesis, melæna, hæmorrhages, and an enlarged liver and spleen are in favour of cirrhosis.

From the effects of backward pressure due to dilatation of the right side of the heart, mitral disease, etc., the diagnosis depends on the recognition of the underlying cause and on the good effects of treatment by cardiac tonics. In cases of adherent pericardium and advanced nutmeg liver (compare "Pericarditic Pseudo-cirrhosis of the Liver," p. 97) the resemblance to chronic perihepatitis associated with adherent pericardium is very close, but cardiac treatment is much more effective in the former condition, which occurs mainly in the young, while universal chronic perihepatitis is little affected by this treatment and usually occurs in adults.

In malignant disease of the liver with ascites there is considerable enlargement of the liver, with perhaps some palpable nodules of new-growth, and the course of the disease is much more rapid.

Syphilitic gummata in the liver may closely imitate perihepatitis by giving rise to recurrent ascites, and the distinction between them is often very difficult. Outward signs of syphilis may be entirely absent, even when there are numerous gummata in the liver. The only reliable means of making a diagnosis is by giving the patient a vigorous antisyphilitic course of iodides.

Chronic Tuberculous Peritonitis.—In this condition the effusion is seldom very large and lumps may be felt in the abdomen. Induration around the umbilicus, concomitant pleurisy, and fever are points in favour of tuberculous peritonitis. In cases of doubt the tuberculin test can be employed.

Prognosis.—The prognosis is most unfavourable: death always occurs eventually, though it may be postponed for a long period. Thus a patient may live to be tapped 60 or even 100 times. But as time goes on the tappings become necessary at shorter intervals, and the patient gradually gets weaker. The disease has been said to be more rapidly fatal in cases associated with adherent pericardium.

Treatment.—Treatment is only palliative. Dry diet, viz., limiting the intake of fluid, and diuretics, such as citrate of caffeine, diuretin, strophanthus, digitalis, apocynum, may be tried. Iodide of potassium is usually given a trial, but it is very doubtful whether it has any effect except when there is syphilitic disease of the liver. However, as the diagnosis between gummata involving the portal vein and universal perihepatitis may be difficult, it is well to give iodides on the chance of an error in diagnosis. Paracentesis should be performed when necessary. a permanent drain is somewhat dangerous from the risk of infection and subsequent peritonitis, and it should therefore not be employed. Hale White * speaks of having tried it without any benefit in one case.

Dissecting off a small piece of the membrane covering the liver and uniting the liver with the abdominal wall, as in Drummond and Morison's operation for cirrhosis, was tried in one case of Dr. Ewart's † by Mr. Warrington Howard in St. George's Hospital, and I believe by others, but without any permanent benefit.

* Hale White: Allbutt's System, vol. iv, p. 123

† Brit. Med. Journal, 1899, vol. i, p. 908.

CIRRHOSIS OF THE LIVER.

CLASSIFICATION OF THE VARIOUS FORMS OF CIRRHOSIS.

Cirrhosis of the liver has been classified in various ways, according to its causes, according to the methods by which the cirrhosis is brought about, according to the anatomical changes and lesions, and according to the distinctive clinical features. Some writers, such as Lancereaux* and Hawkins,† consider cirrhosis under the headings of alcoholic, malarial, and syphilitic. But as there are other factors which may lead to cirrhosis, this classification, though in some ways convenient, is not sufficiently broad.

Classification According to the Methods by which Cirrhosis is Induced.—The following classification of the cirrhoses has been drawn up by Chauffard ‡ and is based on the various methods by which the changes in the liver are brought about:

- I. Vascular.
  - (*a*) Toxic.
    - (i) Poisons taken by the mouth.
    - (ii) Poisons manufactured in the intestinal tract.
  - (*b*) Infective.
    - (i) The direct action of micro-organisms.
    - (ii) The action of bacterial toxines, either produced by bacteria in the liver itself or manufactured elsewhere in the body and carried to the liver.
  - (*c*) Dystrophic.
    - (i) Due to arteriosclerosis; this kind of cirrhotic liver would be homologous to a granular or arteriosclerotic kidney, the fibrosis being a replacement fibrosis.
    - (ii) Due to chronic venous congestion, the fibrosis of a nutmeg liver.
- II. Biliary.
  - (*a*) Secondary to obstruction of the larger bile-ducts.
  - (*b*) Primarily an inflammation of the smallest bile-ducts, leading to a monolobular cirrhosis. Hanot's hypertrophic cirrhosis with chronic jaundice.
- III. Capsular cirrhosis or perihepatitis.
  - (*a*) Chronic localized.
  - (*b*) Chronic universal.

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* Lancereaux: Traité des Maladies du Foie et du Pancreas, 1899.

† Hawkins, H. P.: Allbutt's System of Medicine, vol. iv.

‡ Chauffard, A.: Traité de Médécine [Charcot, Bouchard, Brissaud], vol. iii, p. 827, 1892

This classification is too elaborate, for even from a theoretical point of view the toxic and infective forms overlap, while from a clinical standpoint some of these subdivisions are too minute to be of much practical value.

Anatomical Classifications.—Adami * has proposed a division of cirrhosis on anatomical grounds.

(I) Portal cirrhosis.

(II) Biliary cirrhosis, (*a*) beginning around the larger ducts.
(*b*) beginning around the smallest bile-ducts and capillaries.

(III) Pericellular cirrhosis.

(IV) Arterial cirrhosis; caused by arteriosclerosis inducing a dystrophic cirrhosis or fibrous replacement.

In a microscopic examination of the liver in 100 consecutive cases Adami † found that hepatic arteriosclerosis was by no means uncommon, although it was never marked. Arteriosclerotic fibrosis of the liver might naturally be expected in the aged, and a statement to this effect is sometimes made. Personally from a microscopic examination of a large number of livers I consider it to be very rare, and when present of very slight degree. I have often seen considerable atrophy of the liver cells without any replacement fibrosis.

(V) Centrilobular cirrhosis consisting in fibrous replacement around the intralobular veins and due to chronic venous engorgement.

It has often been assumed that chronic venous engorgement is a cause of fibrosis, and though it is true that some atrophy of the liver cells with a little secondary fibrous replacement is met with, there seems to be no proof at all that chronic venous engorgement of the liver alone gives rise to anything resembling ordinary cirrhosis. Other factors, such as the action of toxines absorbed from the intestines, which are specially prone to catarrh in chronic venous engorgement, may increase this amount of fibrosis. But for practical uses it is safe to state dogmatically that chronic venous engorgement is not a cause of hepatic cirrhosis. This question is discussed under the heading of "Chronic Venous Engorgement" (p. 88).

(VI) Secondary or centripetal cirrhosis is the same as capsular or Glissonian cirrhosis or perihepatitis, which is described elsewhere and is really quite distinct from cirrhosis of the liver.

It is true that a certain amount of fibrosis may spread into the liver substance from the capsule, but the most marked perihepatitis may exist without any trace of hepatic fibrosis; when an extension inwards does occur, the sequence of events is analogous to what occurs in cases of interstitial pneumonia secondary to chronic pleurisy (pleurogenous pneumonia). It has been suggested that toxic bodies manufactured in connexion with the process of perihepatitis may be absorbed by the lymphatics, pass into the liver, and set up fibrosis. If this does occur, its results are comparatively slight and of no practical importance.

(VII) Sporadic cirrhosis. This group includes (i) the fibrosis that occurs locally round miliary or larger granulomata, such as tubercles or gummata, (ii) the fibrosis developing around focal necroses, (iii) fibrosis associated with anthracosis or silicosis. (*Vide* "Pigmented Cirrhosis.") This class is chiefly interesting from an anatomical and pathological standpoint; clinical manifestations are exceptional, but when they are present they resemble those of portal cirrhosis.

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* Adami, J. G.: Sajous' Annual, vol. ii, p. 284, 1899.

† Adami: Montreal Med. Jour., Jan., 1897.

The Author's Anatomical Classification.—A purely structural classification may be drawn up from the microscopic appearances as follows:

(I) *Multilobular cirrhosis* in which a varying number of lobules are enclosed in a fibrous ring; the following sub-varieties may be recognized:
  (*a*) With fatty change in the liver cells.
  (*b*) With hyperplasia of the liver cells to such an extent that nodular cirrhosis, or cirrhosis with adenoma, results.
  (*c*) With pigmentation of the liver cells and also of the fibrous tissues (hæmochromatosis).
  (*d*) Mixed, with pericellular infiltration of the hepatic lobules. This is sometimes seen in rapidly advancing cirrhosis.

Multilobular cirrhosis is almost always due to poisons brought by the portal vein, and is therefore spoken of as periportal or venous cirrhosis, but it may, in exceptional instances, be associated with changes in the larger bile-ducts.

(II) *Monolobular cirrhosis;* each lobule is separated from its fellows by a delicate fibrosis. The arrangement thus far imitates that normally seen in the pig's liver. Monolobular cirrhosis is specially related to inflammation of the minute bile-ducts, but is sometimes described as a result of cholangitis of the larger ducts. Monolobular cirrhosis is often complicated by multilobular cirrhosis and is frequently associated with pericellular cirrhosis, so that a mixed form of cirrhosis results.

(III) *Pericellular cirrhosis;* each hepatic cell is separated by young connective tissue from its fellows.

(IV) *Mixed cirrhosis;* in which there are various combinations of the three preceding main types, the multilobular, monolobular, and pericellular. This is met with in many cases of portal cirrhosis, especially when the course of the disease has been rapid, and is also seen at the termination of long-standing cases of hypertrophic biliary cirrhosis. Mixed cirrhosis is a common anatomical form, but has no claims to be considered as a clinical type of cirrhosis.

(V) *Sporadic fibrosis,* in which there are isolated patches of fibrosis not corresponding with any of the preceding categories. Under this heading come local fibrosis around parasites, cysts, granulomata, the results of small areas of focal necrosis, and the replacement fibrosis seen in chronic venous engorgement.

In the foregoing anatomical classifications the portal and biliary forms of cirrhosis are of great clinical importance, the others, with the exception of pericellular cirrhosis of congenital syphilis and the cirrhosis of hæmochromatosis (p. 300), are chiefly of pathological interest.

Clinical Classification.—If any formal classification be adopted, it should be one that can be used at the bedside. A large number of different varieties of hepatic cirrhosis have been described, and in many cases the probable causes of the cirrhosis, or associated conditions, such as alcohol, malaria, syphilis, tubercle, diabetes, dyspepsia, biliary obstruction, have been taken as grounds for establishing different types of the disease. Again, cirrhosis has been classified according to the size of the liver or of the spleen. A large (hypertrophic) cirrhotic liver and a small (atrophic) cirrhotic liver are often spoken of; while the French school has distinguished different types of biliary cirrhosis not only according to the relation in size between the liver and spleen, but also according to the time incidence of enlargement of the two organs. Thus, the liver may be much larger (hepatomegalic), of relatively much the same size (splenomegalic) or even smaller (hypersplenomegalic biliary cirrhosis) than the spleen; or the liver may be enlarged before (presplenomegalic), at the same time (splenomegalic), or after (metasplenomegalic hypertrophic biliary cirrhosis) the enlargement of the spleen is detected. These titles serve to show the minute and elaborate character of the classification attempted.

A practical classification, which can to some extent be utilized in clinical practice, is that proposed by Senator.

I. Portal Cirrhosis.
  (*a*) The hobnailed liver, diminished in size.
  (*b*) With jaundice, which is either due to gastro-intestinal catarrh obstructing the common bile-duct, or to pressure exerted on the intra-hepatic radicles of the bile-ducts.
  (*c*) With increased size of the liver, which may subsequently be followed by a diminution in bulk.
II. Biliary Cirrhosis.
  (*a*) Due to calculous obstruction of the ducts. No splenic enlargement, no ascites.
  (*b*) With an enlarged spleen. This is a transitional form to the next.
III. Hypertrophic biliary cirrhosis with chronic jaundice.

From a practical point of view it seems to me to be best to make, in the first instance, a broad division of cirrhosis into two principal types as shown by their clinical features:

(*a*) Ordinary or common cirrhosis (portal),
in which hæmatemesis is an early symptom and ascites a terminal incident. Jaundice is not prominent; death may be preceded by a toxæmic state without much or any ascites. The liver may be either large or small, but shows multilobular fibrosis; the spleen is enlarged, but not so constantly or markedly as in the second category.

(*b*) The biliary type. Jaundice is the most prominent feature and may be constant for long periods; hæmatemesis and ascites are only met with exceptionally. A little ascites may develop as a terminal phenomenon shortly before death. The liver is enlarged, sometimes to an extreme degree. The surface is smooth and the fibrosis of a mixed, diffuse, or monolobular type. The spleen is enlarged, sometimes greatly.

In this work these two main types of cirrhosis will be adhered to, but short sections on the subvarieties of cirrhosis, included under these two main types, will be added.

Portal Cirrhosis.
  Variety: Pigmentary Cirrhosis.
Biliary Cirrhosis.
  (i) Hypertrophic Biliary Cirrhosis.
  (ii) Obstructive Biliary Cirrhosis.

Comparison of the Main Forms of Cirrhosis with some Forms of Kidney Disease.—Portal cirrhosis may be compared to a granular kidney. Hypertrophic biliary cirrhosis may be likened to chronic parenchymatous nephritis, the changes being due to poisons reaching the organs by the arterial blood-stream. The terminal production of multilobular cirrhosis in long-standing hypertrophic biliary cirrhosis corresponds to the evolution of a contracting or small white kidney, due to the addition of the changes of a granular or arteriosclerotic kidney to chronic parenchymatous nephritis (large white kidney). Lastly, obstructive biliary cirrhosis is comparable to consecutive nephritis.

PORTAL CIRRHOSIS.

Synonyms: Common, Alcoholic, or Atrophic Cirrhosis, Multilobular, Annular, or Venous Cirrhosis, Laënnec's Cirrhosis, Hobnailed, Gin, or Whisky-drinker's Liver, Chronic Interstitial Hepatitis.

The term atrophic cirrhosis, though commonly used as synonymous with portal cirrhosis, is unsuitable, inasmuch as the liver is often larger than natural. The adjectives portal, multilobular, and common are more accurate. Old names, now forgotten, for the condition are granulated, tuberculated, lobulated liver.

DEFINITION.

The disease is characterised anatomically by fibrosis spreading from the portal spaces and enclosing varying numbers of lobules, in which the cells tend to show degenerative changes. Clinically dyspepsia, hæmatemesis, splenic enlargement, terminal ascites, and œdema of the feet are the essential features, while jaundice is either absent or transient and slight. The disease is commonest about the age of fifty and is frequently related to chronic alcoholism.

HISTORY.

The hardened condition of the liver was described by Vesalius (1514–1564), Harvey, Morgagni, and others. Dr. Payne* in reviewing the history of cirrhosis reproduces the drawing of a cirrhotic liver described in the Philosophical Transactions of 1685 by John Browne, surgeon to St. Thomas' Hospital. The ascites in this case, as in others before this date, was thought to be the result of drinking too much water, a "fault which," according to Dr. Payne, "the bold spirits of the time were much on their guard against." Matthew Baillie * gave a good naked-eye description of the disease under the name of "common tubercle of the liver"; he says it was generally known as a "scirrhous liver," but he regarded it as a disease peculiar to the liver and more apt to occur in those accustomed to drink spirituous liquors.

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* Payne, J. F.: Trans. Path. Soc., vol. xl, p. 310.

The term "cirrhosis" was invented in 1819 by Laënnec,† who regarded the bile-stained "hobnails" as masses of yellow (κιρρός) new-growth, invading the liver, hence cirrhosis. Hanot dutifully proposed that portal cirrhosis should be spoken of as Laënnec's cirrhosis. It is curious to note that in the last quarter of last century the other form of cirrhosis, *i. e.*, hypertrophic biliary, was named after Hanot.

Carswell ‡ in 1838 was the first to point out the presence and importance of fibrosis in cirrhosis, and was confirmed by Kierman's histological researches. Clinically Todd, Murchison, and Hale White's observations have in more recent times advanced our knowledge of the subject. For further details as to the history of cirrhosis the reader is referred to Dr. Wickham's Legg's § essay on this point.

ETIOLOGY.

Age.—Portal cirrhosis is a disease of late middle life and usually proves fatal about fifty years of age.

In 165 adults whose livers were cirrhotic the average age was 48.7 years; of those, 121 were males (average age, 49.4 years) and 44 females (average age, 47 years). In Yeld's ‖ 128 cases the average age was 47.5 years.

There is a definite group of cases of genuine portal cirrhosis in young children, which will be specially referred to elsewhere. (*Vide* p. 332.) The existence of an infantile type of portal cirrhosis, as distinct from biliary cirrhosis and the pericellular cirrhosis of congenital syphilis, has been well established, but the cases are far from common.

Hilton Fagge** found that the average age of persons in whose bodies cirrhosis of the liver was discovered without any marked symptoms during life was five years higher than that of persons dying of the disease. This would tend to show that the compensatory processes had been very successful. My own figures, however, show very little difference between these two classes.

In 78 patients dying from cirrhosis the average age was 48.3 years, while in 87 patients who died from independent causes but whose livers were cirrhotic the average age was 49.1 years.

There is reason to think that cases of cirrhosis with a very distinct alcoholic history are fatal at an earlier age than cases of cirrhosis in which alcoholic excess either did not exist or is not a prominent recent feature in the history. This is especially marked in the case of women.

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* Baillie, M.: Morbid Anatomy, p. 141, 1793.

† Laënnec: Traité de l'auscultation Med., tome i, p. 368, note, 1819.

‡ Carswell: Illustrations of Elementary Forms of Disease.

§ W. Legg: St. Bartholomew's Hospital Reports, vol. vii, p. 74.

‖ Yeld: St. Bartholomew's Hospital Reports, vol. xxxiv, p. 215.

** Hilton Fagge: Guy's Hosp. Reports, Series iii, vol. xx, p. 193.

In 114 cases tabulated by Fenton and myself the average age of all the alcoholic cases of cirrhosis was 46.6 years, as against 49.9 years for the non-alcoholic cases. Taking the ages of the sexes separately, the figures read as follows—alcoholic males, 47.8 years; non-alcoholic males, 49.3; alcoholic females, 42.8; non-alcoholic females, 51.5.

Sex.—Portal cirrhosis is commoner in men than in women; probably in the proportion of about 5 to 2.

In 560 cases where cirrhosis of the liver was found after death, obtained by adding together the statistics of Price, Kelynack, Yeld, and St. George's, there were 412, or 73.6 per cent., in males, and 148, or 26.4 per cent., in females. In a larger number of figures obtained from the bills of mortality of New York for the years 1889–1899, Crook * found that in 4737 deaths from cirrhosis 2980, or 62.3 per cent., were males, and 1757, or 37.7 per cent., females.

From statistics of St. George's Hospital it appears that cirrhosis is more often latent in men than in women. (*Vide* p. 226, "Latency.")

In children some doubt seems to exist as to the sex incidence; in Palmer Howard's † 63 cases males were affected twice as often as females, while Birch-Hirschfeld's statistics were exactly the reverse.

Occupation, etc.—Cirrhosis is more frequent in those who are brought in contact with alcoholic drinks, especially publicans, commercial travellers, and others who have occasion frequently to drink over business or to "treat."

In 149 persons connected with the liquor traffic, Dickinson ‡ found that post-mortem examination showed cirrhosis to occur in 22, while in 149 other persons not brought specially into contact with alcohol it was present only in 8.

Cirrhosis is more often seen in those whose life is sedentary than in persons leading an active outdoor life. Sir D. Duckworth § in 1876 quoted the experience of Sir W. Gull and Sir G. Burrows to the effect that cirrhosis was rare in the upper and well-to-do classes.

Geographical Distribution.—It is an interesting fact that the distribution of cirrhosis does not run hand in hand with that of alcoholism. The abuse of alcoholic drinks is very widespread, but the distribution of cirrhosis does not by any means correspond. Thus, in hot countries alcoholic excess more often tends to produce a rapid reaction in the liver, such as hepatitis, while in cold climates cirrhosis is a more frequent result. But in temperate climates the incidence of cirrhosis varies very considerably; thus, cirrhosis is common in London, but comparatively rare in Scotland. There are also curious differences as to the distribution of cirrhosis in France which cannot be correlated with that of temperance and intemperance. It is an interesting question whether the incidence of cirrhosis has undergone any marked change in the course of years. In 1857 Budd ‖ wrote that "cirrhosis is more common in

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* Crook: Medical News (N. Y.), Feb. 8, 1902, p. 246.
† Palmer Howard: Trans. Assoc. American Physicians, vol. v, p. 1.
‡ Dickinson, W. H.: Trans. Royal Medico-chirurg. Soc., 1873, p. 34.
§ Duckworth: St. Bartholomew's Hosp. Reports, vol. x, 1874.
‖ Budd: Diseases of the Liver, p. 150, 3d ed., 1857.

England and Scotland than in France," while at the present day cirrhosis is probably quite as frequent in France as in England, and much more so than in Scotland. In this connexion it is significant that alcoholism has enormously increased in France of late years.

Heredity.—Multilobular cirrhosis is not a "family" disease or one that tends to recur in members of the same family; in this way it contrasts with hypertrophic biliary cirrhosis, which often attacks several members of the same family. In a few instances several adults may die of alcoholic cirrhosis, probably from a family failing towards alcoholism. In children, the death of two or more members of the same family from multilobular cirrhosis is more often met with. This may depend on hereditary influences, syphilis disposing the organ to the incidence of ordinary cirrhosis—parasyphilitic cirrhosis (*vide* p. 189). An important factor in the development of cirrhosis is the vitality of the liver; if its resistance is congenitally feeble, factors which would otherwise be harmless, such as the poisons of the specific fevers, indiscretions in diet, and so forth, may lead to cirrhosis. It is conceivable that alcoholism in the mother may so influence the livers of her offspring that cirrhosis develops in them more readily than it otherwise would. Precocious alcoholism or peculiarly unsuitable food, such as pickles or fish soaked in vinegar, may be the causes of two or more cases of cirrhosis in the same family. Jollye * described cirrhosis in a brother and sister who had been accustomed to take vinegar. The following cases are interesting in this connexion:

Two sisters, aged nine years and ten years, died in St. George's Hospital in 1899 and 1901 with hobnailed livers weighing 20 and 12 ounces respectively. In both of them laparotomy was performed; in the younger because tuberculous peritonitis was suspected; in the older, who had a temperature of 104° and diarrhœa, because perforation of a typhoid ulcer appeared probable. The mother was extremely alcoholic, but persisted that she had not given alcohol to the children. A brother aged sixteen years was in St. Thomas' Hospital in 1901 and had laparotomy performed for supposed tuberculous peritonitis; no evidence of perihepatitis or peritonitis was found, but there was a hobnailed liver. All three cases died shortly after laparotomy was performed and were examined after death. No abdominal lesion except hepatic cirrhosis was found and no evidence of syphilis was forthcoming in any of them.

THE PATHOGENY OF CIRRHOSIS.

Cirrhosis of the liver is the result of some poison, or possibly of poison-producing bodies, such as micro-organisms, reaching the liver. The factors in question may travel to the liver either (1) by the portal vein, or (2) by the hepatic artery; in other words, they may be derived from the alimentary canal or from the general circulation. When the active agent arrives by the portal vein, the resulting cirrhosis is usually of the ordinary, venous or portal type; when the liver is affected secondary to an arterial infection or toxæmia, the cirrhosis is often of a more mixed type, and may then resemble that of biliary cirrhosis. It is, however, true that in some instances where the poison arrives by the hepatic artery the cirrhosis is of the portal type.

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* Jollye: Brit. Med. Journ., 1892, vol. ii, p. 858.

In reviewing the etiology of cirrhosis it will be convenient, first of all, to consider the poisons and micro-organisms which reach the organ by the portal vein, and then those conveyed by the hepatic artery.

SYNOPSIS.

I.—POISONS CONVEYED TO THE LIVER BY THE PORTAL VEIN.
  (*a*) Ingested poisons: (1) alcohol; (2) other poisons.
  (*b*) Poisons manufactured in the alimentary canal. Dyspeptic cirrhosis.
  (*c*) Umbilical vein cirrhosis and congenital syphilis.
  (*d*) Poisons manufactured in the spleen.
II.—MICRO-ORGANISMS CONVEYED TO THE LIVER BY THE PORTAL VEIN.
III.—POISONS CONVEYED TO THE LIVER BY THE HEPATIC ARTERY.
IV.—MICRO-ORGANISMS CONVEYED TO THE LIVER BY THE HEPATIC ARTERY.
CONCLUSION.

I.

THE POISONS THAT REACH THE LIVER BY MEANS OF THE PORTAL VEIN may be divided into the following categories:

(*a*) The poisons introduced into the intestinal tract from without: (1) alcohol, and (2) other bodies.

(*b*) Those manufactured in the alimentary canal as the result of faulty digestion, fermentation, and putrefaction.

(*c*) The poison of congenital syphilis, conveyed by the umbilical vein.

(*d*) Poisons manufactured in the spleen.

(*a*) INGESTED POISONS.

Of these, alcohol requires much the most consideration and discussion.

(1) *Alcohol and Alcoholic Drinks.*—With regard to the question whether *alcohol* is the cause of cirrhosis, clinical and experimental evidence are hardly in accord. In practice there are few points more certain than that the abuse of alcoholic drinks is a frequent precursor of hepatic cirrhosis, while from experiments on animals the bulk of the evidence is in a contrary direction. In 67 cases of cirrhosis analysed by the Collective Investigation Committee,* 60 per cent. were described as hard drinkers, 30 per cent. as free drinkers, and only the remaining 10 per cent. as fairly temperate.

Among drunkards, however, cirrhosis is not so frequent as is usually assumed. Thus in 250 postmortems on confirmed drunkards who died suddenly from the effects of alcohol, Formad † only found cirrhosis in six. The reason why alcoholics frequently escape cirrhosis is probably either that they have considerable resistance or that some other and necessary factor, which usually accompanies alcoholism, is wanting. The curious contrast between the frequency with which alcoholism appears in the history of cases of cirrhosis and the percentage of cirrhosis in drunkards may perhaps be elucidated by supposing that when the liver is susceptible and likely to suffer from the effect of alcohol it becomes comparatively quickly affected, and that thus before the typical signs of alcoholism have become well marked the case assumes the aspect of hepatic cirrhosis.

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* Collective Investigation Committee's Report upon the Connexion of Disease with Habits of Intemperance, by Isambard Owen, M.D. Brit. Med. Journal, 1880, vol. i.

† Formad: Trans. Assoc. American Physicians, vol. i, p. 225.

There are, of course, many cases of ordinary cirrhosis, especially in children, where alcoholism can be excluded as an antecedent factor in the production of cirrhosis.

Experimentally the introduction of alcohol into the stomach or portal vein of animals has usually given rise to fatty change and sometimes to some necrosis of the liver cells with a little small-cell infiltration around, but in only a few instances has cirrhosis resulted.

Numerous observers, Strassmann,[*] Afanasieff,[†] von Kahlden,[‡] Sabourin,[§] Lafitte,[‖] Pohl,[**] Scagliosi,[††] have perseveringly administered alcohol in considerable quantities to animals over a fairly prolonged period, and have entirely failed to detect any evidence of cirrhosis in the liver.

Straus and Blocq [‡‡] introduced a tube into the stomach of rabbits, and by this means gave 10 grammes of alcohol daily; after three or four months a small-cell proliferation was found at the periphery of the lobules. This is hardly comparable to genuine cirrhosis, and, moreover, the introduction of the tube into the stomach complicates matters, inasmuch as it may have led to catarrh, and thus to the manufacture and subsequent absorption of other irritating bodies. De Rechter [§§] is the only other observer who has seen cirrhosis follow the continued administration of alcohol; he observed it in dogs and rabbits.

Since alcohol alone is not sufficient to account for cirrhosis either in man or animals, the undoubted association between alcoholism and cirrhosis must be explained in some other way. Two possibilities may be referred to: (i) That though ordinary ethylic alcohol itself does not produce cirrhosis, alcoholic drinks in virtue of other bodies contained in them are responsible for cirrhosis. It has been suggested that amylic alcohol is the important factor, but this requires definite proof. Lancereaux[‖‖] believes that sulphate of potash, with which wines in Paris were formerly largely "plastered" (4 to 6 grammes per litre), is the causal factor in the production of cirrhosis, and supports his contention by production of cirrhosis in rabbits, guinea-pigs, and dogs fed on sulphate of potash. The amount of the salt given to these animals was very large, corresponding for an adult man, according to Vallin,[***] to a quantity of 60 to 350 grammes per diem. Viola's[†††] observations on cirrhosis in Venice lent support to the theory that sulphate of potash was an important factor in the production of cirrhosis. Lancereaux's theory, however, is invalidated by the facts that potassium sulphate has not been shown to be present in alcoholic drinks in other countries where cirrhosis is common, and that in 1891 the amount of sulphate of potash allowed to be added to wine in Paris was reduced by the *loi griffe* to 2 grammes per litre; so that, if his theory is correct, cirrhosis ought to have become less common in Paris, which is certainly not the case.

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[*] Strassmann: Vierteljahr. f. gericht. Med., 1888, Bd. xlix, 232.

[†] Afanasieff: Ziegler's Beiträge, Bd. viii, S. 443.

[‡] v. Kahlden: Ziegler's Beiträge, Bd. ix, S. 349.

[§] Sabourin: La Gland Biliare d'Homme, 1888. [‖] Lafitte: Thèse de Paris, 1892.

[**] Pohl: Archiv f. experiment. Path. u. Pharmak., Bd. 31, 1893.

[††] Scagliosi: Virchow's Archiv, September 17, 1896, Bd. cxlv, S. 546

[‡‡] Straus and Blocq: Archiv de Physiol. Norm. et Pathol., 1887, p. 409.

[§§] De Rechter: Bull. Acad. Méd. de Belg., 1892, No. 6, p. 425.

[‖‖] Lancereaux: Bull. de l'Acad. de Méd. Paris, Sept. 7, 1897, t. xxxvii, p. 202.

[***] Vallin: Bull. de l'Acad. de Méd., 1897, t. 38, pp. 285, 343; 1899, t. 39, p. 257.

[†††] Viola: Archiv Gén. de Méd., Jan., Feb., March, 1898, pp. 1, 164, 318.

(ii) According to the other theory, alcohol and alcoholic drinks act in a secondary manner, and either (*a*) set up gastro-intestinal catarrh and thus lead to the production of poisonous bodies which when carried to the liver cause cirrhosis, or (*b*) when acting on the liver simultaneously with bacterial poisons so lower its resistance that cirrhosis results from the effects of the latter.

(*a*) With regard to the first view, Boix has described "dyspeptic cirrhosis," which is not necessarily alcoholic, but is due to the action of fatty acids, such as butyric, lactic, acetic, and valerianic; this he supports by experimental results. Clinically the frequent existence of long-continued dyspepsia is quite in accord with this hypothesis. This point will be referred to later (p. 186).

(*b*) Scagliosi concludes that, while alcohol or bacterial poisons alone do not permanently damage the liver, alcohol may render persistent the lesions induced temporarily in the liver by the poisons of the specific fevers and other infections, and so induce cirrhosis. Ramond * comes to much the same result. He managed to produce cirrhosis by giving alternate doses of bacterial toxines and alcohol by the mouth to animals. He found, by examination of the toxicity of the fæces in man, that alcohol does not necessarily increase the poisonous bodies in the alimentary canal; he was therefore not inclined to support the first view. He believes that alcohol acts as a cellular poison on the liver cells and thus inhibits their special function of destroying poisons brought to the liver. These poisons are then free to induce cirrhosis.

There is not much to choose between these two views, and it is neither necessary nor possible to adopt one exclusively. It is, indeed, not improbable that both of them may be true.

To conclude: with regard to the rôle of alcohol in the production of cirrhosis, it may safely be held that alcoholism is frequently an antecedent condition, but that *per se* alcohol has no specific action on the liver except fatty degeneration. It gives rise to cirrhosis in a secondary manner, either by leading to the production of sclerogenic poisons or by enabling such poisons to have full sway on the liver. The importance of alcoholism has been made rather too much of, and it is not sufficiently recognised that other factors may lead to cirrhosis, and that a congenital or acquired want of resistance on the part of the liver itself is, though hard to estimate, probably of great importance.

(2) *Cirrhosis due to Ingested Poisons other than Alcohol.*—There are numerous cases of undoubtedly non-alcoholic cirrhosis, especially in children. In some of these there has been a definite history of high living and occasionally two or even more members of a family have early in life become affected with hepatic cirrhosis. Cases are on record in which fish pickled in vinegar had been largely taken, while spices, curries, and highly flavoured food have long been thought to account for some cases of cirrhosis. But here it at once becomes evident that it is difficult

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* Ramond: La Presse Médicale, April 21, 1897.

to draw a hard-and-fast line between poisons which are ingested and give rise to cirrhosis by virtue of their own inherent irritating properties, and those factors which set up gastro-intestinal catarrh and by the manufacture of fermentation products inside the alimentary canal lead to what has been termed dyspeptic cirrhosis. Experimentally, it is true, Boix[*] produced some cirrhosis in rabbits by feeding them on acetic, butyric, valerianic, and lactic acids, but these acids are, on the whole, more likely to be produced by fermentation in the human alimentary canal than to be swallowed as such in food. A good example of cirrhosis due to poisonous food is reported by Segers[†] among the Fuegians, who eat large quantities of mussels—from 12 to 25 pounds daily. At a certain stage of their development the mussels are toxic from the presence of myrtilotoxin. As a result of this poison the livers of the Fuegians become enlarged and subsequently cirrhotic and small.

In rare instances cirrhosis has been found to be associated with the presence in the liver, or possibly to be due to the irritation set up by, particles of carbon absorbed from the alimentary canal. This form of cirrhosis—cirrhosis anthracotica—has been seen in connexion with pulmonary anthracosis, and Adami[‡] refers to an analogous form associated with stonemason's lung—silicosis. Lancereaux[§] says it occurs in workers in copper and in coal-miners, and that the intestinal walls are pigmented from the presence of the carbon, this showing the route taken in its absorption. The lymphatic glands in the abdomen are also crowded with particles of carbon. Welch[‖] has also described a case. The records of such cases are few and the amount of cirrhosis comparatively slight; the chief interest is pathological. (*Vide* p. 300.)

Arsenic appears to be capable of setting up cirrhosis of the liver. In the epidemic of arsenical peripheral neuritis due to poisoned beer in the north of England in 1900–1901 quite an unusual number of cases of cirrhosis of the liver and ascites were seen (Reynolds,[**] Sturrock[††]). Hutchinson[‡‡] and Hamburger[§§] have reported ascites in patients who had long been addicted to the medicinal use of arsenic; but in both these instances recovery followed suspension of the drug, so that the existence of cirrhosis was not proved. It has even been tentatively suggested that Banti's disease or the terminal cirrhosis which supervenes in some cases of chronic splenic anæmia is due to the arsenic given medicinally (W. Broadbent[‖‖]). Experimentally cirrhosis has been produced by chronic arsenical and by chronic aluminium poisoning, but cirrhosis in man has not been traced to the latter metal.

In a case of argyria, in which nitrate of silver had been taken for four months for epilepsy, Frommann[*] found early hepatic cirrhosis with deposit of silver.

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[*] **Boix**: Archiv. Général. de Méd., Aug. 6, 1899, p. 210.

[†] **Segers**: La Sem. Méd., 1891, t. xi, p. 448.

[‡] **Adami**: Sajous' Annual, 1898, vol. ii, p. 313.

[§] **Lancereaux**: Traité des Maladies du Foie et du Pancreas, p. 340, 1899.

[‖] **Welch**: Johns Hopkins Hospital Bulletin, 1891, vol. ii, p. 32.

[**] **Reynolds, E. S.**: Medico-chirurg. Trans., vol. lxxxiv, p. 425.

[††] **Sturrock**: Brit. Med. Journ., 1900, vol. ii, p. 1815.

[‡‡] **Hutchinson, J.**: Archives of Surgery, 1895, vol. vi, 389.

[§§] **Hamburger**: Johns Hopkins Hosp. Bulletin, April, 1900.

[‖‖] **Broadbent, W.**: Brit. Med. Journ., 1903, vol. i, p. 1140.

Lead.—Experimentally some slight degree of hepatic fibrosis has resulted from feeding animals with lead (Lafitte[†]), but clinically lead has no claim to be considered a cause of cirrhosis; Lavrand,[‡] indeed, states that the liver is generally unaffected in chronic plumbism. There is, moreover, some doubt as to the mechanism by which lead would produce cirrhosis; perhaps the more probable view is that it leads to arteriosclerosis of the branches of the hepatic artery, and so to slight dystrophic fibrosis.

Naphthol.—By injecting small quantities of naphthol into the portal vein Bouchard[§] produced some fibrosis in the liver.

Bacterial Toxines.—To consider now the effects of bacterial toxines: experimentally Charrin[‖] injected boiled cultures of the Bacillus pyocyaneus into the portal vein, and thus produced extensive small-cell infiltration in the portal canals. Krawkow[**] obtained cirrhosis in birds in similar experiments when prolonged, but Ramond failed to induce cirrhosis in animals by the administration of toxines by the mouth alone, though he obtained positive results where alcohol was given as well.

Krawkow, by introducing cultures of Staphylococcus pyogenes aureus and of other micro-organisms into the alimentary canal produced experimental cirrhosis. The micro-organisms may have merely manufactured a poison, which passed into the portal vein and so to the liver, and set up a purely toxic cirrhosis, but, on the other hand, the micro-organisms may themselves have reached the liver either by the portal vein or by ascending the bile-duct. These points will be referred to later.

(*a*) Cirrhosis due to the Action of Poisons Manufactured in the Intestine.

This theory has already been referred to (*vide* p. 184), in order to explain cirrhosis supervening in alcoholic subjects, where it was suggested that alcohol sets up gastro-enteritis, and thus leads to the formation of poisons which are the direct causes of cirrhosis. Boix[††] and Hanot[‡‡] have described non-alcoholic cirrhosis due to dyspepsia. The liver is first enlarged and tender, and later cirrhosis and jaundice may develop. The cirrhosis ascribed to gout may be of this nature, while the non-alcoholic cirrhosis in Mohammedans and the natives of India and Egypt, a form long ago referred by Budd[§§] to the action of spices, curries, and other stimulating articles of food, such as ginger, may be explained as depending on the irritating effects of acetic, butyric, lactic, or other acids manufactured as the result of intestinal fermentation. Cirrhosis of this kind is sometimes described as due to auto-intoxication or as autochthonous, and in a posthumous article by Hanot[*] was called "Budd's cirrhosis." In order to meet the obvious objection that dyspepsia is comparatively seldom followed by cirrhosis, Boix argues that the resistance of the liver is an important factor, and that where this is congenitally feeble continued dyspepsia will lead to cirrhosis. This idiosyncrasy or predisposition is included under the French term "arthritism."

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[*] Frommann: Archiv f. path. Anat. u. Physiol., Berlin, Bd. xvii.

[†] Lafitte: Thèse de Paris, 1892.

[‡] Lavrand: Le Néphrite des Saturnines, p. 12, 1899.

[§] Bouchard: Therapeutics des Maladiès Infectieuses, p. 313, 1889.

[‖] Charrin: Archiv de Physiol. Norm. et Path., 1893, p. 554.

[**] Krawkow: Archiv. de Med. experiment. et d'Anat. Path., vol. viii, p. 268.

[††] Boix: La foie des dyspeptics, Thèse de Paris, 1894. Archiv. Général. de Méd., Aug., 1899, p. 210.

[‡‡] Hanot and Boix: Congrès de Rome, 1894.

[§§] Budd: Diseases of the Liver, p. 151, 1857.

In cases of long-standing mitral disease hepatic fibrosis may be due to several causes. A certain degree of fibrous replacement as a result of atrophy of the liver cells may occur. An explanation of this "cardiac cirrhosis," which may be appropriately mentioned here, is gastro-intestinal catarrh; this gives rise to the formation of irritating bodies which, when absorbed, find the liver in a condition of diminished resistance and are thus able to set up inflammatory changes. It may be noted, however, that the fibrosis secondary to chronic venous engorgement, however produced, is slight and of no real clinical importance. (*Vide* "Chronic Venous Engorgement.") The ascites often accompanying backward pressure is nearly always the result of concomitant chronic peritonitis.

Among the children of Brahmins around Calcutta, and probably elsewhere in India, a peculiar form of cirrhosis described as intercellular and perilobular, or "biliary," has been described.[†] It occurs usually when the infants are about eight months old, and about 95 per cent. of those who suffer from it die before the end of the second year. It is very apt to occur in the same family; thus, no less than fourteen children of the same parents have died of it one after the other. There is no evidence that it is syphilitic; it is ascribed to bad milk, faulty digestion, and to poisonous products generated in the intestines. The mothers' milk is not improbably the causal factor, as they restrict themselves to a dry diet and take a decoction of black pepper. Whether the poisons are introduced in the food or formed in the infant's intestines it is impossible to say; perhaps both methods obtain, but the latter is the more probable of the two.

Among Brahmins and other high-class Hindus who, as a rule, lead abstemious lives and never touch alcohol, cirrhosis of the liver is of frequent occurrence (Young[‡]). Ginger-eating is a prevalent practice with them and they are addicted to cardamoms, red pepper, and other hot spices. The cirrhosis may well be secondary to dyspeptic changes thus induced in the alimentary canal. In Egypt cirrhosis is found among Mahommedans, who take no alcohol, and may possibly be due to anchylostomiasis and the production of toxines inside the intestine, since slight cirrhosis has been found in the bodies of persons affected by anchylostomiasis and bilharzia.

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[*] Hanot: La Cirrhose de Budd, Archiv. Général. de Méd., 1899, p. 3.

[†] J. B. Gibbons: "Scientific Memoirs by Medical Officers of the Army of India," Part vi, 1891, The Indian Lancet, May, 1896, p. 426. Togendro Nath Ghose: Lancet, 1895, vol. i. E. Mackenzie: Lancet, 1895, vol. i. Nil Ratan Sircar: The Indian Lancet, July 1, 1896.

[‡] Young, L. T.: Carlsbad Treatment, p. 129, 2d ed., 1899 ("Ginger Liver").

In typhoid fever[*] necrotic areas of small size, focal necroses, "lymphomata," or "lymphoid nodules," as they have been variously called, are often met with. The liver cells first degenerate and subsequently a certain amount of small-round-cell infiltration surrounds the necrotic areas. It is conceivable, therefore, that under favourable conditions a sporadic multiple fibrosis may result throughout the liver; usually these lesions are recovered from. Some observers have regarded typhoid fever as a starting-point for cirrhosis. It is possible that if alcohol is taken and the resistance of the liver thus further diminished, this change may be rendered permanent. If this be so, it is desirable that some caution should be maintained in giving stimulants during convalescence. From Reed's careful observations it appears probable that these focal necroses are due to toxalbumins conveyed to the liver and that these areas do not contain typhoid bacilli. Hanot has found similar nodules in the liver in cases of tuberculous enteritis. According to Mallory,[†] two distinct lesions have been described under the term lymphoid nodules: (1) a focus of lymphoid and plasma cells confined to the connective tissue around the portal vessels and independent of the liver cells; (2) focal necrosis of cells in hepatic lobules due to blocking of capillaries by proliferated and phagocytic cells.

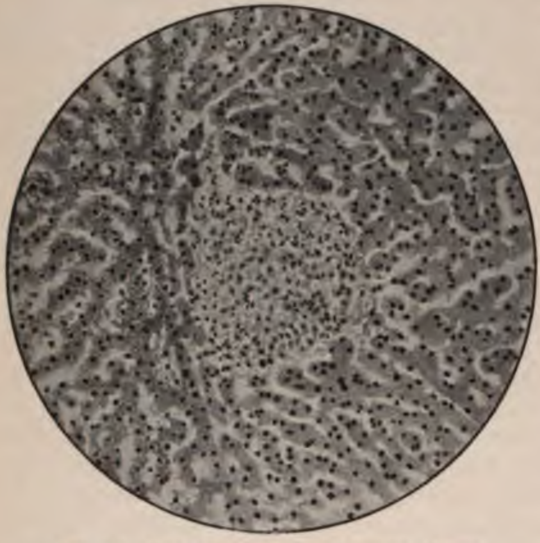

FIG. 25.—FOCAL NECROSIS IN TYPHOID FEVER. The liver cells around the area of necrosis show pigmentation. × 110.

Cirrhosis has been regarded as a late result of cholera, and it seems reasonable to believe that the slightly increased fibrosis around the portal spaces sometimes seen in rickets is due to gastro-intestinal catarrh giving rise to the manufacture and absorption of poisonous bodies which pass up to the liver by the portal vein. The question also arises as to what part prolonged diarrhœa and gastro-enteritis in children may play in the development of cirrhosis. It is conceivable that toxines absorbed in the course of appendicitis * may imitate cirrhotic changes in the liver. In pernicious anæmia where a poison is probably absorbed from the intestinal tract and carried to the liver no cirrhosis results. Possibly the organ is in such a poor state of nutrition that it is incapable of any inflammatory reaction. The same explanation has been invoked to account for the absence of fibrosis in lardaceous disease of the liver. (Kanthack.†)

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[*] Friedreich: Virchow's Archiv, Bd. xii, S. 53. Reed: Johns Hopkins Hospital Reports, v, p. 379. Handford: Trans. Path. Soc., vol. xl, p. 129. Hanot: C. R. Soc. de Biolog., p. 856, 1893. Siredey: Rev. de Méd., t. vi, 1886. Legrey: Thèse de Paris, 1892. Amyot: Canadian Practitioner, January, 1898.

[†] Mallory: Journ. Experim. Med., vol. iii, p. 622.

By intraperitoneal injection of a micro-organism allied to the colon group Weaver ‡ obtained cirrhosis in guinea-pigs, but the micro-organism was not found in the liver, hence the change in the liver may be regarded as due to the toxines absorbed into the portal vein.

(c) UMBILICAL VEIN CIRRHOSIS.

In *congenital syphilis* the blood, presumably containing the toxine, arrives by the umbilical vein and thus passes into the branches of the portal vein in the liver. Here the poison reaches the liver by the portal vein, being derived from the placenta which, in the fœtus, functionally represents the intestine. The resulting lesion is a diffuse pericellular cirrhosis. In exceptional instances a similar change is found in acquired syphilis; but with these exceptions syphilis does not directly produce hepatic cirrhosis, though it may lead to local fibroses, gummata, and cicatrices. Though this is undoubtedly true, it appears that pericellular cirrhosis, which is a secondary lesion of syphilis and thus curable, often leaves behind it a deficient resistance on the part of the liver and thus disposes it to become cirrhotic in the ordinary way. I have seen several cases of well-marked cirrhosis of the common type in the subjects of congenital syphilis, and therefore believe that indirectly syphilis plays a part in the incidence of cirrhosis. In other words, congenital syphilis so prepares the soil that cirrhosis of the ordinary type may supervene. Under these conditions the cirrhosis may be regarded as a parasyphilitic lesion.

Other poisons, besides that of syphilis, may travel from the mother to the fœtus by the umbilical vein and give rise to changes in the liver. Our knowledge of umbilical vein cirrhosis is extremely meagre, but it is reasonable to believe that the disease known as congenital obliteration of the bile-ducts may start in the liver and be due to toxines conveyed there by the umbilical vein, and that the subsequent obliteration of the ducts is a later and secondary change due to a descending cholangitis.

(d) POISONS MANUFACTURED IN THE SPLEEN.

In hæmic infections micro-organisms tend to accumulate in the spleen, and, if not rapidly destroyed, produce toxines which travel to the liver and may there produce changes analogous to cirrhosis. Chauffard § has argued in favour of cirrhosis being in some cases secondary to morbid processes originating, or at any rate most marked, in the spleen. Thus, in malaria the spleen is greatly enlarged and cirrhosis of the liver in malarial subjects may in part be due to poisons manufactured in the spleen. In chronic splenic anæmia it may sometimes happen that a terminal cirrhosis of the liver with jaundice occurs; this has been termed Banti's disease, and is regarded by Chauffard as a good example of cirrhosis of splenic origin. The difficulty is to be sure the cirrhosis has not existed throughout.

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* Tuffier et Mauté: La Presse Méd., p. 408, June 29, 1904.
† Kanthack, A. A.: St. Bartholomew's Hosp. Journ., Nov., 1896, vol. iv, p. 22.
‡ Weaver: Philadelphia Med. Journal, Feb. 4, 1899, p. 283.
§ Chauffard: Sem. Méd., p. 177, 1899.

As will be seen in the description of hypertrophic biliary cirrhosis, the typical monolobular cirrhosis is very frequently obscured by the addition of multilobular cirrhosis. This latter change may be explained as due to the infective agent, which primarily reached the liver by the hepatic artery and sets up monolobular cirrhosis, settling down in the spleen and producing toxines which, when conveyed by the splenic vein to the liver, induce multilobular cirrhosis. In support of the theory that poisons are manufactured in the spleen and conveyed to the liver is the fact that endophlebitis of the splenic vein has been described in malaria by Kelsch and Kiener,* in enteric fever by Bezançon,† and in splenic anæmia.

The portal vein may indeed be regarded as having two main sources in adult life—(*a*) the gastro-intestinal veins, by which poisons commonly travel to the liver, and (*b*) the splenic vein. In fœtal life the umbilical vein is a third distinct tributary and may also convey poisons to the liver.

A point of speculative interest in connexion with cirrhosis of the liver due to poisons manufactured in the spleen arises from Sérégé's ‡ view, based on injection experiments with methylene-blue, that the blood from the spleen goes exclusively to the left lobe of the liver. If this is true, cirrhosis due to poisons produced in the spleen should be confined to, or chiefly in evidence in, the left lobe of the liver. I am not aware that there is anything in support of this to be found in literature.

At present the existence of hepatic cirrhosis as a sole result of poisons manufactured in the spleen requires further investigation, but it is an attractive idea and is compatible with the fact that in one variety of hypertrophic biliary cirrhosis, the so-called metasplenomegalic, the spleen is enlarged before there is any manifest change in the liver.

II.

MICRO-ORGANISMS ABSORBED FROM THE ALIMENTARY CANAL.

Cirrhosis thus produced would be described as septic or infectious in contradistinction to toxic cirrhosis, which is due to the action of poisons without the presence of microbes in the liver. Such a suggestion is highly probable, but cannot be accepted at present. Adami,§ while investigating the Pictou cattle disease, found intercellular or pericellular cirrhosis accompanied by swelling of the peri-portal and retro-peritoneal lymphatic glands, and œdema of parts of the intestine. These lesions were associated with a minute bacillus belonging to the colon group. Adami has found the colon bacillus almost constantly in human livers. When the livers are healthy, the bacilli appear to have been killed by the bactericidal action of the liver cells. In progressive cirrhosis there are, in addition to dead bacilli, some areas where they appear active. This suggests the possibility that virulent colon bacilli may under conditions of diminished resistance of the liver cells, such as may be induced by alcohol, lead to cirrhosis. Adami [*] considered that a primary inflammation of the alimentary canal favoured invasion of the liver by the bacilli which set up cirrhotic changes in that organ.

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* Kelsch and Kiener: Traité des Maladies des Pays chaudes, p. 405, 1889.
† Bezançon, F.: Thèse de Paris, 1895.
‡ Sérégé, H.: Journ. de Méd. de Bordeaux, May 25, June 1, 8, 1902.
§ Adami: Brit. Med. Journ., 1898, vol. ii, p. 1215.

It is, *a priori*, extremely probable that an acute hepatitis due to the brunt of a hæmic infection falling on the liver would, if not fatal, leave behind it hepatic cirrhosis. Cases in human beings occur where a febrile condition, accompanied by enlargement and tenderness of the spleen and liver, ushers in and precedes an illness which eventually is seen to have for its chief anatomical lesion a cirrhotic liver. At present the sequence of microbic hepatitis resulting in ordinary cirrhosis, though highly probable, cannot be regarded as resting on a sufficient basis of fact. Some fibrosis is seen in prolonged cases of acute yellow atrophy.

In a boy, aged sixteen years, death occurred fourteen days after the onset of measles. Roger and Conte [†] found that an acute localized enteritis in the ileum had given rise to hepatitis, inflammation between the liver and diaphragm, an acute rapid putrid effusion into the right pleura, and, finally, gangrene of the lung. The bacillus found resembled the B. coli. The liver showed masses of round-celled infiltration in the portal spaces, degeneration of the liver cells, cholangitis, and endarteritis. The process was very acute, but it makes it easy to understand that a slighter degree of the same process, if recovered from, might be the starting-point of cirrhosis.

By intraperitoneal injections of cultures of a bacillus belonging to the pseudo-diphtheria group Hektoen [‡] produced cirrhosis of the liver in animals. The bacilli were found in the capillaries of the liver.

Experimentally by introducing cultures of micro-organisms into the intestines of birds Krawkow sometimes found that cirrhosis developed, but the result may have been merely due to their toxines being carried to the liver, and there is no evidence that in his experiments the micro-organisms themselves travelled to the liver.

It is possible that in some exceptional instances tubercle bacilli carried from the intestines to the liver may set up some degree of cirrhosis. Hanot and Gilbert's [§] experiments show that avian tubercle bacilli may induce cirrhosis in guinea-pigs, and they believe that this sclerogenic result depends either on relatively high resistance on the part of the liver or on a slight degree of virulence on the part of the bacilli. As a rule, of course, tubercle bacilli either give rise to tuberclic or to degenerative changes in the liver cells. As a curiosity reference may be made to bilharzia passing up the portal vein and giving rise to

[*] Adami: Report of Minister of Agriculture for the Dominion of Canada for year 1901, p. 135.

[†] Roger and Conte: La Presse Médicale, Sept. 29, 1897.

[‡] Hektoen: Journ. Path. and Bacteriol., vol. vii, p. 214.

[§] Hanot and Gilbert: Soc. de biolog., Jan. 30, 1892.

cirrhosis.[*] According to Kartulis,[†] the liver is usually enlarged in size and there are no symptoms of cirrhosis.

III.

Cirrhosis due to Poisons in the General Circulation which Reach the Liver by the Hepatic Artery.

This cirrhosis may be spoken of as toxic and due to the action of poisons on the liver. It has been suggested that cirrhosis may be set up by the specific fevers, typhoid fever, scarlet fever, measles, and variola, and pneumonia. Theoretically, the toxines of these diseases may, when absorbed into the general circulation, set up focal necrosis of the liver cells, and under certain conditions fibrosis might develop around these areas of necrosis.

Focal necrosis may occur in typhoid, scarlet fever, measles, variola, and diphtheria. In cases of typhoid fever the poison might reach the liver by the hepatic artery and give rise to focal necrosis. Klein [‡] and Crooke [§] described acute interstitial hepatitis in scarlet fever, and more recently Pearce [‖] has met with focal necroses of the liver cells; this is analogous to scarlatinal nephritis, but it probably is a transient condition and clinically there is little relation between scarlet fever and hepatic cirrhosis. Focal necroses in measles have been described and figured by Freeman.[**] Small-cell accumulations, like those produced in typhoid fever, have been described in the liver in variola by Roger and Weil.[††] Arnaud,[‡‡] who describes in addition small-cell infiltration near the portal spaces, suggests that cirrhosis may subsequently follow.

In diphtheria focal necroses occur and are described by Councilman, Mallory, and Pearce [§§] as being situated round the intralobular vein. There are degeneration of the liver cells and some proliferation of the endothelium. These changes are due to the action of poisons and not to the presence of diphtheria bacilli in the liver. Weaver[‖‖] injected a micro-organism allied to the colon group into the abdominal wall of guinea-pigs and produced local abscesses in which the bacilli were found, none being present in the liver, which showed focal necroses and cirrhosis. It is reasonable to believe that as the result of other local infections focal necroses in the liver may be produced, and that under favourable conditions some sporadic fibrosis might develop around these foci. The question whether absorption from tuberculous pulmonary vomicæ which are secondarily infected with streptococci can induce cirrhosis is referred to elsewhere.

[*] Symmers Jour. Path. and Bacteriol., vol. ix, p. 237.

[†] Kartulis: Sem. Méd., 1894, p. 415.

[‡] Klein: Trans. Path. Soc., vol. xxviii, p. 439.

[§] Crooke: Birmingham Med. Review, vols. xx, xxi.

[‖] Pearce: Boston (U. S. A.) City Hosp. Reports, 1899, p. 74.

[**] Freeman: Medical Record, July 28, 1898. Pediatrics, Feb., 1900.

[††] Roger and Weil: Soc. de biolog., Nov. 2, 1900.

[‡‡] Arnaud: Marseille Médical, 1899, p. 39.

[§§] Councilman, Mallory, Pearce: Diphtheria, a study of 220 fatal cases, Boston, U. S. A., 1901.

[‖‖] Weaver: Philadelphia Med. Journ., Feb. 4, 1899.

The conditions favouring the development of permanent cirrhosis after infections are congenital susceptibility or want of resistance on the part of the liver, and the presence of other factors, such as alcoholism. In the rare condition of hæmochromatosis, in which there is widespread pigmentation of the body, the liver becomes first infiltrated with pigment and then cirrhotic; the liver cells degenerate and become pigmented. The pancreas is similarly affected, and when a certain degree of intensity is reached, diabetes results. This constitutes bronzed diabetes. Of 30 cases of hæmochromatosis 5 only have not shown diabetes. It is noteworthy that in the cirrhotic livers of hæmochromatosis there is endarteritis of the hepatic artery; this suggests that there is some additional factor associated with the process of hæmolysis which causes the change in the liver cells and the cirrhosis. Thus the cirrhosis seen in hæmochromatosis may possibly be due to a poison reaching the liver by the hepatic artery, which, as Adami points out, is probably of bacterial origin.

Experimentally, a certain amount of hepatic fibrosis has followed prolonged poisoning with vegetable, mineral, and bacterial poisons. The intoxication must be induced gradually and continued for a considerable period. If the poison is employed in too large amounts, the results are those of acute poisoning, viz., degeneration and necrosis of the liver cells, focal or diffused, as in phosphorus poisoning. In the same way, the injection of bacterial poisons into the circulation, when carried on rapdily, gives rise to necrotic changes in the liver cells around the intralobular veins; when the process is less intense and more prolonged, a certain amount of cirrhosis results. Krawkow * obtained positive results with sterilised cultures of Bacillus pyocyaneus, and Claude † with diphtheritic toxine. But it is probable that these effects are transitory, and do not, when uncomplicated (*vide* p. 184) by alcoholism, give rise to cirrhosis in man. Flexner,‡ in a careful study of chronic intoxication by ricin and abrin,—vegetable alkaloids or phytalbumoses,—produced a form of cirrhosis. As a result of injection of phosphorated oil into the subcutaneous tissues of rabbits, Aufrecht § found that the liver cells showed degenerative changes and that later some small-cell infiltration took place around the lobules. Other poisons, when injected into the circulation, such as carbonate of ammonia, indol, skatol, phenol, sulphonal, have also led to a slight degree of microscopic fibrosis.

IV.

CIRRHOSIS DUE TO MICRO-ORGANISMS IN THE GENERAL CIRCULATION REACHING THE LIVER AND THERE PRODUCING POISONS THAT SET UP CIRRHOSIS.

In hæmic infection the liver changes are often extremely acute and give rise either to suppuration or to widespread degenerative changes allied to acute yellow atrophy. In less acute hæmic infections the supporting fibrous tissues show proliferation and accumulation of leucocytes in the portal canals and in the peripheral parts of the lobules of the liver. These changes are the same as those seen in the acute specific fevers, such as variola, scarlet fever, etc. (*Vide* p. 192.) Occasionally in pyæmia and septicæmia, due to streptococci, staphylococci, etc., as in acute necrosis, infective endocarditis, puerperal septicæmia, and erysipelas,[*] considerable small-cell infiltration of the liver is met with.

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* Krawkow: Archiv de Méd. expériment et d' anat. path., vol. viii, p. 269, 1896.

† Claude: Thèse Paris, 1897.

‡ Flexner: Journ. Experiment. Med., vol. ii, p. 19, 1897.

§ Aufrecht: Deutsch. Archiv. f. klin. Med., 1897.

In the hepatitis due to repeated attacks of malaria there is considerable damage done to the liver cells, as shown by focal necroses (Barker[†]), and fibrous hyperplasia is sometimes seen. The actual importance of malaria as a cause of cirrhosis appears to be surprisingly small. (*Vide* p. 305.)

Typhoid fever has already been referred to as leading to small necrotic areas in the liver (p. 188). In ordinary typhoid fever these nodules appear to be due to the action of toxines conveyed from the alimentary canal, and not to bacilli. But in cases of general typhoid septicæmia, where there may be no intestinal lesions, infection of the liver by the hepatic artery is possible. In fifteen cases of this kind collected by Bryant,[‡] typhoid bacilli were recovered from the liver in four cases. The changes in the liver due to general hæmic infections are probably usually recovered from if the patient lives, but should conditions arise which depress the resistance of the liver, such as alcoholism, cirrhosis might conceivably result.

Experimentally there is some evidence that hæmic infections may induce hepatic cirrhosis. Krawkow[§] injected cultures of various micro-organisms into the muscles of fowls and pigeons, and found that after a considerable interval hepatic cirrhosis developed. This was especially well marked when the Bacillus pyocyaneus and the Staphylococcus pyogenes aureus were employed. By subcutaneous injection of cultures of a bacillus belonging to the pseudo-diphtheria group, Hektoen[‖] obtained well-marked portal cirrhosis in animals.

It must, however, be remembered that in chronic hæmic infections the spleen becomes crowded with micro-organisms, and that if they multiply there, toxines may be manufactured in considerable quantities and carried by the splenic and portal veins to the liver, and there set up a cirrhosis of splenic origin. (*Vide* p. 189.)

CONCLUSION.

Experiment shows that a large number of poisons are capable of giving rise to changes in the liver comparable to those of cirrhosis. Often, it is true, these lesions are early, or, at the best, not well marked. But the facts are of value as indicating that cirrhosis in man may reasonably be considered as the result of a toxic process. These poisons may be absorbed either from the alimentary canal, and then reach the liver in a comparatively concentrated form, or they may travel to the liver by the hepatic artery; the dose is then comparatively dilute as compared with the former class. Ordinary cirrhosis in man is generally due to poisons travelling by the portal vein. Alcoholism is rather an antecedent condition than a *causa vera*, and acts indirectly or in an accessory manner; though in ordinary practice the association between cirrhosis and antecedent alcoholism is of fundamental importance. The possibility of cirrhosis being definitely due to micro-organisms is one that must be faced; from analogy it is most probable, but at present, as in the case of syphilis, it has not been certainly established. It is also highly probable that poisons, or perhaps micro-organism, reaching the liver by the hepatic artery may give rise to changes of a cirrhotic nature. The mechanism of this change will be further referred to in the section on "Hypertrophic Biliary Cirrhosis."

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[*] Roger and Garnier: Rev. de Méd., March, 1901.

[†] Barker: Johns Hopkins Hosp. Reports, vol. v.

[‡] Bryant, J. H.: Brit. Med. Journ., 1899, vol. i, p. 778.

[§] Krawkow: Archiv de Méd. expérim. et d' anat. path., tome viii, p. 268.

[‖] Hektoen: Journ. Path. and Bact., vol. vii, p. 214.

NATURE OF THE FIBROSIS OF CIRRHOSIS.

It is perhaps most widely held that cirrhosis is primarily and essentially a chronic inflammation or hyperplasia of the connective tissue in the portal areas, and that the atrophic and degenerative changes in the liver cells are either (i) entirely secondary and due to pressure exerted by the contracting fibrous tissue, or to impaired nutrition from curtailed blood supply, or (ii) unimportant and almost accidental concomitant phenomena.

Powell White * has gone to the opposite extreme and suggested that large smooth cirrhotic livers are not due to inflammatory processes, since they show none of the contraction which is so characteristic of inflammatory hyperplasia and to a lesser extent of replacement fibrosis. His view is that there is a diffuse fibroma of the liver.

The alternative view is that cirrhosis is essentially a replacement fibrosis and is secondary to a primary degeneration and atrophy of the liver cells. Payne † and Lionel Beale regarded cirrhosis as essentially an atrophic change. On the theory that it is a replacement fibrosis the changes in cirrhosis of the liver would be regarded as analogous to those in systemic sclerosis of the spinal cord or to those in an arteriosclerotic kidney.

Against this it may be urged—

1. That extensive atrophy or degeneration may occur without any fibrosis resulting. Thus, in old age there may, as I have seen, be marked atrophy of the cells in the peripheral zone of the hepatic lobule, with little or no fibrosis. In lardaceous disease, and in universal fatty change, there may be complete freedom from fibrosis. In reply, it may be said that in such cases there is a general debility of the whole organ, and that the fibrous tissues share in it, and are therefore unable to undergo proliferative changes. (Kanthack.‡)

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* Powell White: Brit. Med. Journ., 1900, vol. ii, p. 1057.

† Payne, J. F.: Trans. Path. Soc. London, vol. xl, p. 321, 1889.

‡ St. Barth. Hosp. Journ., London, Nov., 1896.

2. That, microscopically, the proliferation of the connective tissues is so exuberant, so exactly like those of active inflammation elsewhere, and the degenerative changes in the cells so slight in comparison, that it is difficult to believe that the latter changes can be primary. In such cases there may well be two factors at work, namely, proliferation of the connective tissues and degenerative changes in the liver cells, and both may be due to the simultaneous action of the toxine. But, while bearing this explanation in mind, it must be remembered that a replacement fibrosis shows itself, not only as a passive overgrowth, but as a proliferation, for, both in degenerative "neuritis" and in granular kidney (arteriosclerotic in origin), much small-cell proliferation may sometimes be seen.

3. That inasmuch as cirrhosis is, in ordinary conditions, due to the action of a poison, it is reasonable to believe that the effects will be no more limited to the hepatic cells than to the fibrous tissues, as was formerly supposed to be the case. In other words, that the parenchymatous and interstitial changes are both, in the first instance, due to the same cause, and therefore vary directly in intensity. If this be so, it is easy to understand that the hepatic cells, being more sensitive, will react before the more resistant connective tissue, and that degenerative changes in them will usually, for this is their usual method of reacting, precede hyperplasia of the connective tissues. There are further grounds supporting the view of a simultaneous reaction on the part of the liver cells and framework as the starting-point, or first stage at any rate, in some cases of cirrhosis. In multiple adenoma or nodular cirrhosis the liver cells may actively proliferate, and so give rise to the so-called adenomata, while at the same time there is fibrosis. This process might perhaps be regarded as a general hyperplasia, and many cirrhoses, such as the nodular cirrhosis sometimes met with in the subjects of malaria or tuberculosis, might be spoken of as hypertrophies that failed.

The so-called new bile-ducts, or pseudobile canaliculi, met with in Hanot's hypertrophic cirrhosis with chronic jaundice, in ordinary cirrhosis, around hepatic gummata, etc., are, as Dreschfeld * pointed out years ago, due to active proliferation of the liver cells, and may be regarded as an attempt, not, it is true, entirely successful, at compensatory hyperplasia of the liver cells.† But it is important to bear in mind that there are possibly, if not probably, different ways in which the fibrosis of cirrhosis is brought about, and that the causative factors may vary during the course of an individual case. Thus, while the changes may at the outset both be the result of the toxine, irritative hyperplasia in one case, degeneration in the other, subsequently one of these changes may react on the other process. Thus, the products of the degenerating liver cells may act as a further irritant and stimulus to the fibrosis, and, conversely, the presence of fibrosis may hamper the nutrition of the liver cells. As Adami ‡ has pointed out in discussing

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* Dreschfeld: Journ. Anat. and Physiol., London, vol. xiv, p. 69

† Hanot: Gaz. d. hôp., Paris, July 10, 1896.

‡ Montreal Med. Jour., Dec., 1896.

the etiology of cirrhosis, there is a tendency for secondary changes to occur in the course of cirrhosis, so that a pure venous cirrhosis starting from the portal vein readily spreads to the bile-ducts, and sets up changes in them, and a mixed form of cirrhosis results.

In conclusion, it is, in the present state of our knowledge, safest not to regard the cirrhotic process as exclusively due either to irritative hyperplasia of the connective tissues, the hepatic cells being quite passive, on the one hand, or to primary degenerative or atrophic changes in the hepatic cells with a resulting replacement fibrosis on the other, but to steer a middle course, and to remain content with the view that the irritating poisons leading to cirrhosis affect both elements in different ways, and that the resulting changes in one tissue may further initiate fresh changes in the other tissue, or modify those already existing.

MORBID ANATOMY.

Size and Weight.—The size of the liver in ordinary cirrhosis may vary very greatly; it may be smaller than natural, and is then often spoken of as "atrophic," and in extreme instances may not weigh more than 30 ounces; or, on the other hand, it may be extremely large and weigh as much as 150 or 200 ounces. It is noteworthy that a cirrhotic liver which is actually smaller than natural often weighs as much as a healthy liver or even more, its specific gravity being much increased. There are transitions between a small and a large multilobular cirrhotic liver, but they all belong to the same category of disease. It is undesirable to speak of the small ones as "atrophic" and the large ones as "hypertrophic" cirrhosis, since the practice of calling a large multilobular cirrhotic liver "hypertrophic" has been the cause of much confusion with hypertrophic biliary cirrhosis.

The large size of some cirrhotic livers may be due to considerable fatty change in the liver cells. It has been assumed, I believe quite incorrectly, that increased size and fatty change in cirrhosis are especially connected with over-indulgence in malt liquors rather than in spirits.

Some years ago these points were considered in the course of an analysis of 114 cases of cirrhosis undertaken by Fenton and myself.* Taking an equal number of alcoholic cirrhotic livers from cases in which malt liquors on the one hand and spirits on the other had been chiefly drunk, there was found to be very little difference between the average weights of the livers in the two series. The number of cases available was very small, since in most of the 114 cases where the form of stimulant taken is mentioned, both beer and spirits were taken. In 10 beer livers the average was 69 ounces, and in 10 spirit livers 67 ounces. The spirit livers appeared to be more frequently fatty. The number of cases is so small that no stress can be laid on these figures; they are mentioned, however, because an analysis of Foxwell's cases does not support, in fact militates against, the commonly received opinion that a beer drinker's liver is, as a rule, large, and a spirit drinker's liver small.† In a series of microscopic examinations it was found rather unexpectedly that fatty change occurred in an equal proportion in large and in small cirrhotic livers, and that half the large livers examined did not show fatty change.

In cirrhosis complicating pulmonary tuberculosis the liver is usually somewhat enlarged from fatty change. As will be shown later (p. 199), the liver is larger in cases of cirrhosis where the disease is latent and death occurs from some independent cause than in those cases that die directly from cirrhosis. The enlargement is chiefly due to compensatory hyperplasia of the liver cells, but there may be considerable fatty change in the hepatic cells; this form had been specially described by Hanot and Gilbert * as "hypertrophic alcoholic cirrhosis." In other instances the large size of the liver is due to the fibrosis having a smaller mesh and approaching a monolobular type or showing that arrangement in parts. Enlargement of a cirrhotic liver is often temporary and due to congestion, either active, when the cirrhotic process is progressing, or passive, and due to backward pressure from dilatation of the heart.

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* Rolleston and Fenton, W. J.: Birmingham Med. Review, Oct., 1896, p. 198.

† Foxwell, A.: Birmingham Med. Rev., April, 1896, p. 221.

In cases dying from the effects of cirrhosis the liver is larger in younger subjects than in those of more advanced years. There are grounds for thinking that in patients dying from cirrhosis in whom no alcoholic history is forthcoming, the liver is smaller than in the more familiar type of alcoholic patients dying from cirrhosis.

In 6 cases in which cirrhosis was fatal and in which there was no evidence of alcoholic excess the average weight of the liver was 41 ounces, whereas in 36 fatal cases of alcoholic cirrhosis, the average weight was 67.7 ounces.

In cases of latent cirrhosis the liver is a little larger in patients addicted to alcoholic excess than in the non-alcoholic, but the difference is very small as compared with that mentioned above in patients dying from the effects of cirrhosis.

In 29 cases where death was due to some other cause and the evidence of alcoholic excess was forthcoming, the average weight of the cirrhotic liver was 62.2 ounces, while in 26 cases where alcoholic cirrhosis was latent the average weight of the liver was 67.9 ounces.

Sex does not seem to exert any very special influence on the size and weight of the cirrhotic liver.

In 116 men the average weight of the cirrhotic liver was 61.5 ounces, or 8½ ounces in excess of 53 ounces, the normal weight, while in 41 females the average weight was 55.5 ounces, or 10 ounces in excess of the normal weight, 45 ounces. Hale White † examined 50 cases to see whether large or small cirrhotic livers were commoner in women, and found that large cirrhotic livers were rather more frequent in women.

The large cirrhotic livers are less knobby than the smaller examples which especially merit the title hobnailed.

When both the liver and the spleen are much enlarged, the left lobe of the liver may touch or overlap the spleen. This is much more likely to occur in hypertrophic biliary cirrhosis, but I have seen it in undoubted multilobular cirrhosis.

The weight of the liver in portal cirrhosis may be diminished, normal, or increased, but it is less often below than above or of the normal weight.

In 142 cases tabulated by Price ‡ the liver was less than the normal weight in 27 per cent.

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* Hanot and Gilbert: Soc. Méd. des Hôp. Paris, May 23, 1890.

† Hale White: Guy's Hosp. Gaz., May 27, 1898.

‡ Price: Guy's Hosp. Reports, series iii, vol. xxvii, p. 295.

My own statistics show a very considerable increase in the weight of the cirrhotic liver, but in 100 cases collected by Hawkins * the average weight was 52 ounces, and in 93 tabulated by Kelynack † 53 ounces, which is very close to Reid's average weight for the normal liver (53 ounces for males, 45 ounces for females). The average weight of the liver in cases dying from the effects of cirrhosis appears to be less than that of patients with latent cirrhosis who die from independent causes.

In 155 consecutive postmortem examinations on patients with cirrhotic livers at St. George's Hospital the average weight was 63.6 ounces. Of these, 75 died from the effects of cirrhosis, the average weight of the liver being 60 ounces, while the average weight of the liver in the remaining 80 patients who had cirrhotic livers but died from other causes was 67 ounces. In 11 of the 142 cases tabulated by Price death was due to accident, and the average weight of these cirrhotic livers was 76 ounces.

In latent cirrhosis the weight of the liver diminishes as age advances; this is probably a senile atrophic change. In this connexion it is interesting to note that in cases of latent cirrhosis in fatal granular kidney, which is perhaps a premature senile change, the weight of the liver is not increased.

Thus, in 8 cases of combined hepatic and renal cirrhosis examined at St. George's Hospital the average weight of the liver was 56.5 ounces, the average age of the patients being 52.25 years, or 3.5 years above the average age at death in cirrhosis. Pitt's ‡ figures pointed to the same conclusion, but Price's figures, also from Guy's, tended to show that granular kidney was associated more often with a large than with a small cirrhotic liver.

In cases dying from cirrhosis the weight of the liver becomes less as age advances; this, again, may be partly due to the advance of years.

Morbid Appearances in the Liver.—The peritoneal surface of the liver is opaque; this may be due to chronic peritonitis, which is sometimes (*vide* p. 222) associated with cirrhosis. Not uncommonly there is more thickening of the peritoneum over the liver than elsewhere. The opacity of the capsule is, however, largely due to subcapsular fibrosis and atrophy of the liver cells, which, though it gives somewhat the same naked-eye appearance, is essentially quite different from genuine perihepatitis. It is probable that chronic perihepatitis is often described when subcapsular fibrosis is the actual condition present. This opacity is not uniform; it is more marked between the projections or hobnails, where there is underlying fibrous tissue.

General perihepatitis occurred in 15 out of 53 cases of cirrhosis recorded by Cheadle,§ or 28 per cent., and in 13 out of 78 autopsies tabulated by Sears and Lord,‖ or 16.6 per cent.

There may be adhesions between the liver and adjacent parts, especially between its convexity and the diaphragm. These adhesions may be dense, but are often comparatively delicate. They may be remarkably vascular. The surface of the organ is irregular; the projections vary in size from a pea to that of a pigeon's egg. When they are small, the surface of the organ somewhat resembles that of a granular kidney, and the term "granular liver" is applicable. When, as more rarely occurs, the hobnails are large, the organ may look as if it was occupied by numerous secondary growths, especially when the projections show marked fatty change and appear white, though it is worthy of note that the hobnails never show the umbilication usually present in secondary carcinoma. When the projections are exceptionally large, the condition is sometimes spoken of as nodular cirrhosis or cirrhosis with multiple adenoma.

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* Hawkins: Allbutt's System, vol. iv, p. 174.

† Kelynack: Birmingham Med. Review, Feb., 1897.

‡ Pitt, G. N.: Trans. Path. Soc., vol. xl, p. 348.

§ Cheadle, W. B.: Lancet, 1900, vol. i.

‖ Sears and Lord: Boston Medical and Surg. Journ., vol. cxlvii, p. 285.

Occasionally in an otherwise uniformly cirrhotic liver there is one large prominent hobnail; this has been described, rather unnecessarily, as solitary adenoma with cirrhosis. It is probable that this condition is of the same nature as multiple adenomata in cirrhosis, but differs in there being only one area of marked hyperplasia. Caminiti* has described two examples of solitary adenoma with cirrhosis.

The hobnails are of a tawny yellow or brown colour, being often stained by bile; the peritoneum over them sometimes shows dilated vessels. During life the liver looked uniformly red in the laparotomies on cases of cirrhosis I have seen. The capsule, which is not much thickened as a rule, is more opaque in the depressions between the nodules. Usually the liver is uniformly affected, especially when it is enlarged and the nodules are small, but the change may be irregular and the left lobe is often in a more advanced condition and may be very small. It is possible that the resistance of the left lobe is less than that of the right, for it is not infrequently more affected in acute yellow atrophy (*q. v.*) than the right. Sometimes, on the other hand, one of the smaller lobes, such as the spigelian or caudate, may be enlarged out of proportion to the others, even when the organ as a whole is little, if at all, bigger than normal.

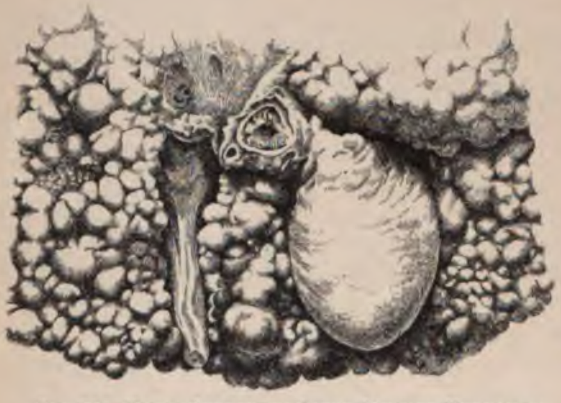

FIG. 26.—UNDER SURFACE OF LIVER SHOWING HOBNAILED APPEARANCE.
The portal vein is thrombosed. (Drawn by Dr. E. A. Wilson.)

On section the liver is tough and like a section of conglomerate stone being divided up into areas of irregular size by grey, slightly gelatinous-looking, fibrous tissue. The interlobular tissue in cases of very marked cirrhosis may have a red, somewhat spongy appearance and be rather depressed, as compared with the masses of liver tissue that are embedded in it and stand up on section on a higher level. This fibrous tissue is

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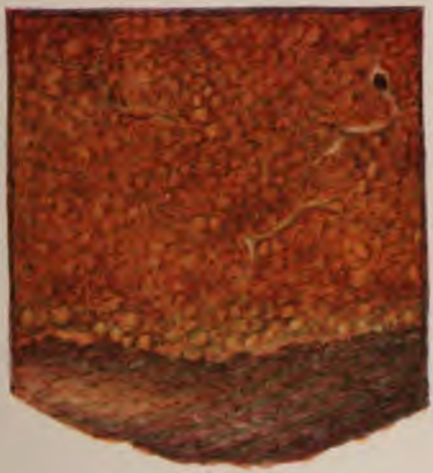
* Caminiti: Archiv f. klin. Chirurg., 1903, S. 630.

PLATE 2.



PORTION OF A FINELY GRANULAR CIRRHOTIC LIVER SHOWING THE SURFACE AND THE SECTION.
Dr. E. A. Wilson.

continuous with the depressed, more opaque areas on the capsule, and by its contraction has squeezed into prominence the more healthy parts of the liver, which thus form the nodules or hobnails.

This fibrosis spreads out from the medium-sized portal canals and exerts its constricting influence on the branches of the portal vein. This is shown by the difficulty of injecting the hepatic capillaries from the portal vein. The areas of liver substance thus enclosed vary in size, being usually from $\frac{1}{6}$ to $\frac{1}{4}$ inch in diameter, and contain six to ten lobules, each of which normally measures $\frac{1}{20}$ to $\frac{1}{16}$ inch in diameter. The liver substance is much paler than in health and has a yellowish brown colour either from staining with bile or from fatty change. In the same liver the colour of different hobnails often varies, some being yellow, others of a brownish-red colour. This may be due to irregularity in the amount of fatty change.

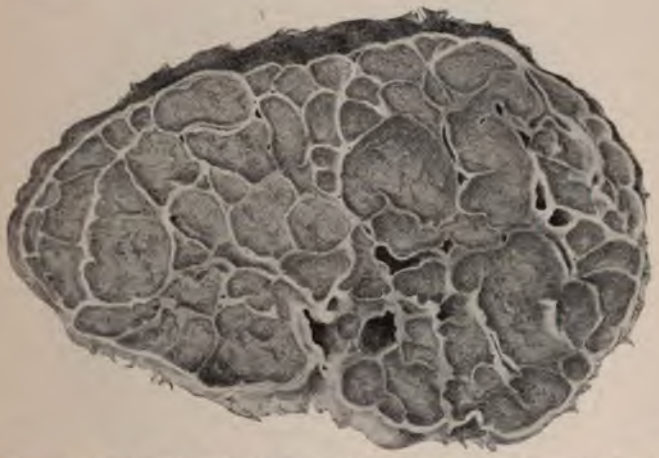


FIG. 27.—SECTION OF MULTILOBULAR CIRRHOTIC LIVER SHOWING IRREGULARITY IN THE MESH OF THE FIBROUS TRABECULÆ. (Drawn by Dr. E. A. Wilson.)

Occasionally hæmorrhages are found in the interstitial tissue, in the hobnails, or in both. The liver cells may be compressed by the extravasated blood and sometimes show necrosis. When the hæmorrhage is widespread in the interlobular tissue and the hobnails have undergone fatty change, an appearance exactly like new-growth may be produced. The hæmorrhages may possibly be due to the toxic condition of the blood, but this is unlikely, since hepatic hæmorrhages are rare in fatal cases of cirrhosis, where death is usually due to toxæmia. In some instances it is due to fatty change in the cells in the hobnails removing the support of the contained vessels; while Bonone * has suggested that endarteritis of the hepatic artery may produce necrosis of the liver cells and hæmorrhages. As a coincidence I have seen numerous hæmorrhages into the cirrhotic liver of a man who died from hæmatemesis. Occasionally small thrombosed veins may be seen in the liver without any similar change in the

* Bonone: Quoted Rev. Génér. de Path. Intern., 1900, p. 70.

portal vein or its larger branches. It has been suggested that thrombosis of the terminal branches of the portal vein may determine ascites, but there is no proof that there is any relationship between the two events; as a matter of fact, thrombosis of the smaller veins is seldom observed.

Histology.—In the early or more progressive stages there is small-cell infiltration in and around the portal spaces; these cells are due to hyperplasia of the existing connective tissues of Glisson's capsule and to some leucocytic invasion. In a well-marked case there is an irregular meshwork of connective tissue extending throughout the liver and dividing it up into variously sized islands of liver tissue. Inasmuch as a number of lobules are enclosed within the same fence of connective tissue, the term multilobular cirrhosis is applied. The number of lobules enclosed in different compartments differs; in some parts there are many, in other areas a single lobule or half a lobule is separated off from the rest.

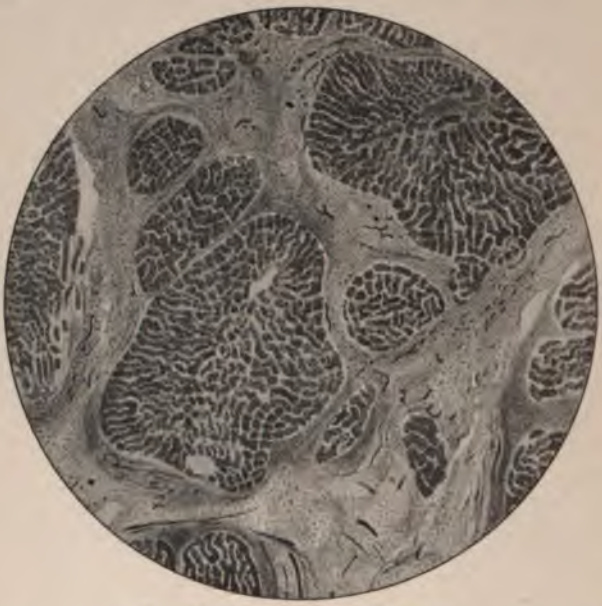


Fig. 28.—Multilobular Cirrhosis.

Well-formed fibrous tissue separating off masses of liver cells of various sizes. The normal arrangement of the liver cells is lost. In the fibrous tissue there are a few "newly formed bile-ducts."

The French school considers that the fibrosis is not only portal, but also around the sublobular veins or bivenous. (Sabourin.*) It is true that the pressure of the surrounding trabeculæ may obliterate the intralobular veins, and by condensation and contraction so alter the appearance of the enclosed lobules that it is difficult to count the number enclosed in the alveoli of the connective tissue, but it does not appear, at any rate to me, that there is fibrosis around the intralobular veins. At the margin of the lobules the fibrous tissue can be seen to surround bits of the lobule and thus to shave off groups of cells from the edge of the lobule. In some large cirrhotic livers, where the meshwork is still multilobular as a whole, there are parts where it is more diffuse and approaches the monolobular type; this condition of mixed cirrhosis is, from an anatomical point of view, a transitional stage to hypertrophic biliary cirrhosis; but it is quite commonly seen in ordinary portal cirrhosis when the disease is rapidly advancing.

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* Sabourin: Revue de Méd., 1882, p. 465.

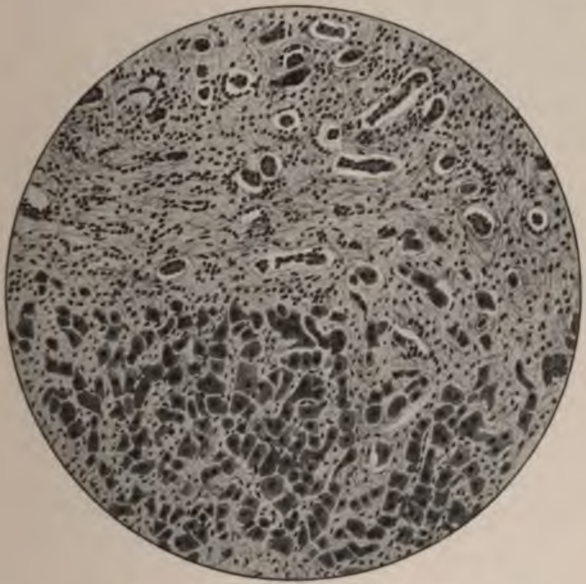

FIG. 29.—MULTILOBULAR CIRRHOSIS.

Shows invasion of a lobule by young connective tissue, so that there is local intercellular cirrhosis. Some of the liver cells thus isolated show hypertrophy and are beginning to divide and form columns of small cells—"the so-called new bile-ducts." The older connective tissue has some so-called new bile-ducts in its meshes. × 140.

When the morbid process is progressing rapidly the lobules are often actually invaded, so that a certain amount of intercellular fibrosis is superadded. It thus often happens that the liver of portal cirrhosis shows a very mixed cirrhosis, there being areas of monolobular and intercellular cirrhosis in addition to the prevailing multilobular type. It is not justifiable or necessary, however, to attempt to construct a special clinical type of mixed cirrhosis to correspond to these microscopic appearances. The nature of the fibrous tissue varies according to its age, and whether the process is progressing or stationary. There is nearly always some well-formed fibrous tissue containing small round and spindle cells. In cases running a rapid course the amount of small round cells is increased, while in latent or stationary cases there may only be old fibrous tissue. The interstitial tissue contains numerous newly formed vessels derived from the hepatic artery, which are sometimes much dilated.

The increase in connective tissue was formerly assumed to consist solely of white fibrous tissue derived from proliferation of the preexisting tissue in the portal canals. Recent histological methods show that there is an increase in the amount of elastic tissue.

Hohenemser,* in 1895, using Unna's acid orcein stain for elastic tissue, showed the presence of elastic fibres in the connective tissue of portal cirrhosis; this has been confirmed by Melnikow-Rasnednekow † and Flexner.‡ The elastic tissue spreads out from the sheaths of the hepatic artery, portal vein, and bile-duct, and is also found in the capsule. More elastic tissue is found in cases of portal cirrhosis than in biliary and mixed forms of cirrhosis.

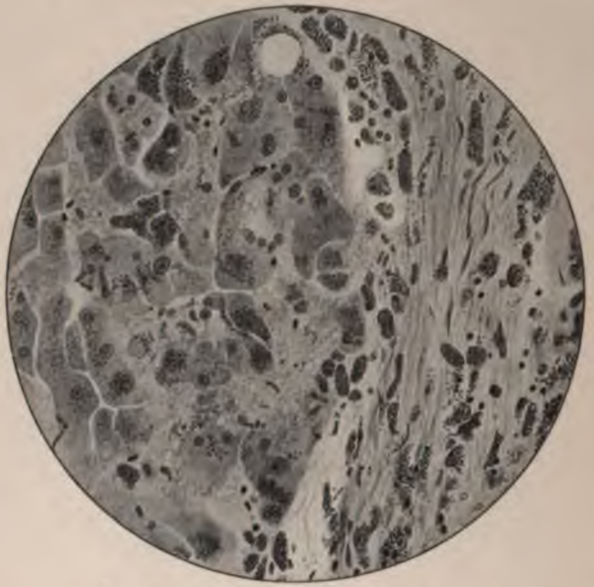

FIG. 30.—CIRRHOSIS IN HÆMOCHROMATOSIS.

Section at margin of lobule. Shows hæmosiderin as dark granules in the liver cells and also in the fibrous tissue surrounding the lobules. Prepared from Dr. Maude Abbott's case. (*Vide* Trans. Path. Soc., vol. li, p. 56.) × 220.

In pigmentary cirrhosis (*vide* p. 299), which may be due to more than one cause, the fibrous tissue may become occupied by opaque masses of pigment. In hæmochromatosis, where there is a liberation of hæmoglobin from the red blood-corpuscles in the general circulation with a deposit of blood-pigment in the cells of the liver, pancreas, and other glands, and an accompanying fibrosis, the pigment is eventually liberated from the liver cells and passes into the connective tissues.

Pigmentation of the fibrous tissue in cirrhosis is also seen in malaria and in the extremely rare condition of cirrhosis anthracotica. (*Vide* p. 185.)

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* Hohenemser: Virchow's Archiv, Bd. cxl, S. 192, April 2, 1895.

† Melnikow-Rasnednekow: Ziegler's Beiträge, Bd. xxvi, S. 526.

‡ Flexner: University Medical Magazine, Philadelphia, Nov., 1900, p. 613.

Newly Formed Bile-ducts—Pseudobile Canaliculi.—The interstitial tissue shows as a prominent feature columns of small cells which stain deeply, show karyokinesis, and are therefore in a state of active growth. The cells are small and may be cubical, but are often elongated so as to

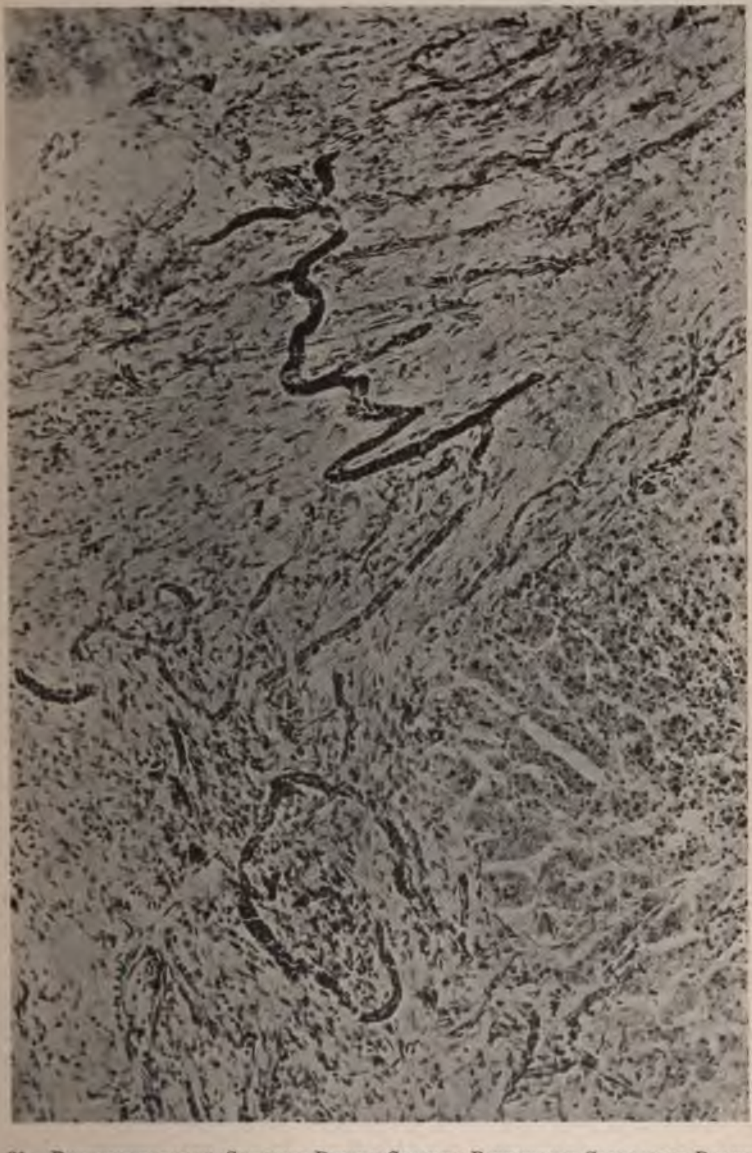

FIG. 31.—PHOTOMICROGRAPH SHOWING DEEPLY STAINED PSEUDOBILE CANALICULI BRANCHING AND TWISTING IN THE FIBROUS TISSUE.

The margin of a lobule is also shown. From a case of multilobular cirrhosis. (Dr. H. R. Spitta.)

lie in the long axis of the column; they are arranged on much the same pattern as in a small bile-duct around a potential lumen. It is indeed open to doubt whether similar structures containing a dilated lumen or masses of inspissated bile are exactly the same as these so-called new bile-ducts; possibly the former are pre-existing bile-ducts. The so-called new bile-ducts twist and branch in the interlobular connective tissue and form a rough network. The individual columns catch one's eye as minute worm-like bodies under a low power.

Special importance was formerly attached to the presence of these so-called new bile-ducts in hypertrophic biliary cirrhosis, but they may be just as prominent in common cirrhosis, and indeed are present in a number of conditions, such as local fibrosis around a hydatid cyst, gumma, in tubercle, lymphadenoma, acute yellow atrophy, and other lesions which have in common destruction of the liver cells.

A considerable amount of discussion has arisen as to their nature. It has been thought that they are the pre-existing bile-ducts of the portal spaces and lobules of the liver which are left in a conspicuous position by the atrophy and recession of the liver cells; the brilliant staining of the cells is explained by supposing that some proliferation of the cells normally lining the ducts in the interlobular tissues around the portal canals extends into the flat-walled ducts between the liver cells. Against this view are the facts that in senile or other forms of simple atrophy of the liver cells the appearance of so-called new bile-ducts is not seen, and that histologically they differ from normal bile-ducts in that they either have no elastic fibres or only an imperfect development of these fibres around them. (Flexner.*) From their resemblance to small bile-ducts it has naturally been suggested that they are due to proliferation of pre-existing bile-ducts, but this is chiefly based on the facts that they are usually prominent features in cases of biliary cirrhosis and have been observed after experimental ligature of the ducts. Against this are the facts that these so-called new bile-ducts are seen in very diverse conditions which only resemble each other in destroying the liver cells, and that the bile-ducts may be little or not at all affected when these so-called new bile-ducts are present.

Another suggestion is that the liver cells become surrounded by the advancing fibrous tissue, which, so to speak, slices off columns of hepatic cells from the periphery of the lobules. (*Vide* Fig. 28.) The liver cells then atrophy, become compressed, and are said to revert to the type of a tubular liver. This view as to the nature of the change is supported by some appearances, but is opposed to the fact that they stain deeply and are evidently actively proliferating. It seems more probable that they are, as pointed out by Dreschfeld † years ago, the result of active proliferation of the liver cells, and, as Hanot ‡ believed, an attempt at compensatory hyperplasia. The healthy liver cells proliferate in order to compensate for the destruction of the hepatic tissues. Appearances strongly suggesting hyperplasia of the cells may be seen at the periphery of the lobules, and the columns of small cells may in fortunate sections be traced into continuity with a liver cell. Since at any rate considerable doubt exists as to their being bile-ducts, it is more convenient to speak of them as the so-called new bile-ducts or pseudobile canaliculi.

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* Flexner: University Medical Magazine, Philadelphia, 1900, p. 617.
† Dreschfeld: Journal of Anatomy and Physiol., vol. xiv, p. 69.
‡ Hanot, V.: Gaz. des Hôp., Paris, July 10, 1896.

The liver cells in the early stages may show little or no change, and in cases where the disease has become latent or compensated they may be larger than natural from compensatory hypertrophy. When the disease is well established or advanced, changes in the cells are the rule. The normal trabecular arrangement in the lobule is disturbed by the circumferential pressure exerted by the contracting fibrous tissue, and disappears. In some cases, owing to backward venous pressure from cardiac failure, the capillaries between the columns of liver cells become dilated and separate single columns of cells from each other. In other cases the lymphatic capillaries are dilated and the lobule becomes œdematous. When cirrhosis is advanced, the liver cells show degenerative changes. Fatty change is often present in a greater or lesser degree, and is the effect of the action of alcohol or some other toxic substance, It has been thought that fatty change is specially related to excess in beer and other sugar-containing beverages, but, plausible as it appears, this assumption has not been proved. (*Vide* p. 197.)

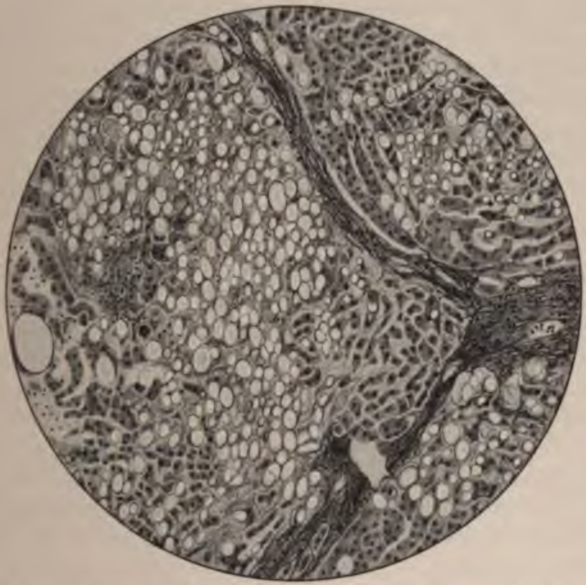

FIG. 32.—SLIGHT MULTILOBULAR CIRRHOSIS WITH EXTENSIVE FATTY CHANGE IN THE LIVER CELLS.

The vacuolation of the liver cells is irregular. Some groups of cells are unaffected, while others have hardly any of their protoplasm left. × 72.

The degenerative changes are extremely marked in those cases which run a rapid or an acute course. The protoplasm may show cloudy swelling and become granular, while the nucleus may stain badly or be obscured. The presence of pigment granules of bile is seen in cases where jaundice has existed, while in malaria, hæmochromatosis, and in other examples of pigmented cirrhosis (*vide* p. 299) the liver cells are crowded with pigment and are markedly degenerated.

The liver cells may show hæmosiderosis quite apart from the existence of general hæmochromatoses.

In 16 cases of cirrhosis Abbott* found pigment in the liver cells in 6 cases, and in 26 cases examined by Kretz† pigmentation existed in 14. Since this pigment is probably due to the hæmolytic action of intestinal bacteria, it is curious that it is not more constant in cases of cirrhosis.

In the early stages of cirrhosis a majority of the liver cells, even those cut off and embedded in fibrous tissue, contain glycogen. This observation of Brault's ‡ helps to explain the absence of glycosuria in cases of cirrhosis. He suggests that in cirrhosis there may be excessive glycogen storage in the liver cells in order to bring about compensation for the cellular destruction.

Compensatory hyperplasia of the liver cells in cirrhosis occurs in two forms: (i) the earlier, or the so-called new bile-ducts already described, and (ii) the change which when fully developed gives rise to the multiple adenomata. In both, the proliferation of the liver cells begins at the margin of the lobule, probably because the blood-supply to the cells is more copious there. In the form of compensatory hyperplasia giving rise to multiple adenomata the liver cells become individually larger and show karyokinesis, multiply, and lead to an increase in the size of the lobules and to the formation of actively growing masses of liver tissue. Many of the "hobnails" in a cirrhotic liver are of this nature. When the process is well marked, the condition is called nodular cirrhosis, or cirrhosis with adenoma. This process is of great importance in compensating for the destruction of the liver cells and allowing the disease to become latent.§

Gall-bladder and Bile-ducts.—The gall-bladder and larger bile-ducts do not show any constant change to the naked eye. In some instances the walls of the gall-bladder are thickened from past or from chronic cholecystitis, and occasionally there is inflammation of the larger ducts. In cases where ascites is present the serous coat of the gall-bladder may be œdematous.

Gall-stones occur slightly more frequently in cases of cirrhosis than in the ordinary run of cases. Thus, in 136 cases of cirrhosis examined after death at St. George's Hospital gall-stones were found in 21, or 15.4 per cent.; but in many of these cases there were only small calculi in the gall-bladder, and in a few only bilirubin-calcium calculi.

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* Abbott, M.: Trans. Path. Soc., vol. li, p. 79.

† Kretz: Beiträge zur klin. Med. und Chir., Heft 15, 1896, Wien.

‡ Brault: Archiv de Méd. expériment. et d'Anatom. path., tome xiv, p. 453, 1902. La Presse Médicale, May 29, 1901. Bull. Soc. Anat. Paris, 1901, p. 334.

§ Hanot et Gilbert: Bull. de la Soc. Méd. des Hôp., 1896, p. 492.

The small intra-hepatic bile-ducts are usually healthy or show little change. In some instances there is concomitant catarrhal cholangitis.

In one case microscopic sections of a cirrhotic liver with some perihepatitis showed cystic dilatation of the bile-ducts in a few of the portal spaces. It is indeed remarkable how extremely rare any dilatation of the small ducts is in cirrhosis, especially in view of the frequency of cysts in a granular kidney, which may be considered as an homologous condition to hepatic cirrhosis.

Portal Vein.—The intra-hepatic branches of the portal vein are compressed, and in rare instances are thrombosed. The trunk of the portal vein and its branches are dilated, and very occasionally varicosities are seen on its mesenteric radicles. The walls of the vein are thickened by periphlebitis and there is opacity of the intima from endophlebitis; in extreme instances secondary calcification may occur in the intima. These changes are comparable to arteriosclerosis and are connected with increased pressure in the portal vein, or possibly with the presence of poisons in the blood. Thrombosis of the trunk of the portal vein is more often associated with hepatic cirrhosis than with any other condition, but it is a rare complication, occurring in about 3 per cent. of the fatal cases of cirrhosis.

In a remarkable case of calcification of the portal and splenic veins in a man whose case is referred to on page 81, the liver showed old, non-progressive cirrhosis of the liver.*

Dilatation of the Communications between the Portal Vein and the General Systemic Veins.—This is important as providing a collateral circulation for venous blood which would otherwise have to force its way against the obstruction offered by the cirrhotic liver. On the development of this compensatory anastomosis great importance is laid as one of the factors which enable cases of cirrhosis to become latent or to appear cured. The normal communications between the portal vein radicles and the general systemic veins are (i) general, and (ii) local.

(i) *General communications* between the retroperitoneal veins, opening into the lumbar, azygos veins, etc., and the veins of the peritoneum and of the intestines occur especially where, as in the case of the duodenum, pancreas, ascending and descending colon, areas drained by the portal vein are bound down to the abdominal parietes. The veins in the fat around the left kidney anastomose to some extent with the veins of the descending colon, and venous trunks may put the renal vein itself into communication with the colica sinistra vein. The veins of the descending colon may communicate with the spermatic plexus, and this has been thought to favour the development of varicocele on the left side. (Bennett.†) Compensatory dilatation of this anastomosis has been recorded, but in general it is of little or no importance. It has not appeared to me that varicocele is specially common or marked in patients with cirrhosis.

A communicating branch between the splenic and the left renal veins has been seen, and in Jacobson's‡ case of compensated hepatic cirrhosis, in which death occurred from uræmia due to granular kidneys, a vein as large as the thumb ran from the left renal vein into the trunk of the portal vein. A somewhat similar anastomosis has been observed by Virchow* between the splenic vein and the azygos vein.

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* Trevor, R. S.: Trans. Path. Soc., liv, p. 302.

† Bennett, W. H.: On Varicocele, p. 43, 1891.

‡ Jacobson, G.: Archiv. Général. de Médecine, 1893, vol. i, p. 353.

In some cases of cirrhosis the greater part of the parietal peritoneum, more especially on the posterior wall and upper part of the abdominal cavity, is markedly injected and in some areas resembles a "claret stain" on the skin. The significance of this, and also the fact that it is not due to a terminal peritonitis, are shown by the absence of this injection from the peritoneum covering the free coils of the small intestine. This subperitoneal plexus of anastomoses has been described by Retzius, after whom it is sometimes called, while Sir W. Turner † specially investigated the anastomoses between the visceral and parietal arteries. Peritoneal adhesions around the liver, stomach, omentum, or spleen may become markedly vascular and thereby assist the collateral circulation.

This hint on the part of nature has been taken in a surgical sense by Drummond and Morison,‡ who artificially produced adhesions between the liver and abdominal wall, and by Talma,§ who sutured the omentum to a wound in the abdominal wall, and thus led to a diminution of ascites.

(ii) *Local.*—(*a*) Around or in connexion with the liver: communications may develop between the veins in the substance and capsule of the liver and the phrenic and intercostal veins, where the liver and diaphragm are uncovered by peritoneum, *i. e.*, between the layers of the coronary ligament and its lateral fringes, the lateral ligaments.

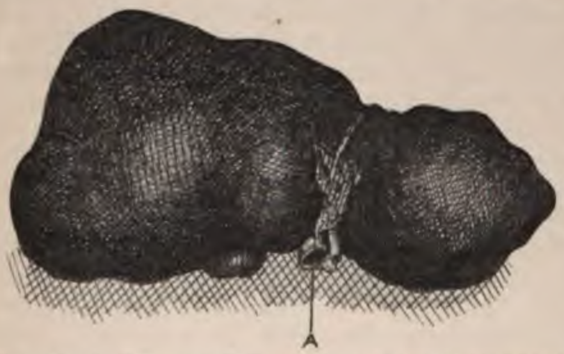

Fig. 33.—A Cirrhotic Liver with a Large Parumbilical Vein (A) in the Falciform Ligament. The round ligament is also shown. (Drawn by L. Jones, M.B., F.R.C.S.)

The falciform ligament of the liver may contain a large vein which runs to the umbilicus and may communicate there with the veins of the abdominal wall, and so establish a communication between the portal vein in the transverse fissure of the liver and the deep epigastric and external iliac veins. This vein is comparable with the epigastric vein of cold-blooded air-breathing vertebrates, such as the frog. This vessel may be a greatly dilated parumbilical vein, which, according to Luschka, normally puts the portal and epigastric veins into communication, and runs alongside of the obliterated umbilical vein. On the other hand, this vein may be the umbilical vein, which has become pervious again and, so to speak, has reverted to its fœtal function of carrying blood, with the difference that the blood runs away from, instead of to, the liver. Sappey * insisted that the large vein found in the falciform ligament in some cases of cirrhosis was always independent of the umbilical vein, but this is not in accord with cases quoted by Champneys.†

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* Virchow: Quoted in Frerichs' Diseases of Liver, vol. ii, p. 41. Transl. New Sydenham Soc.

† Turner, W.: Brit. and Foreign Medico-chirurg. Review, vol. xxxii, p. 222.

‡ Drummond and Morison: Brit. Med. Journal, 1896, vol. ii, p. 479.

§ Talma: Berlin. klin. Wochenschrift, Sept. 19, 1898, S. 833.

This vein may be extremely large; Wilks ‡ mentions a case where it was as big as the portal vein, and in Sappey's case and the case figured here it admitted the little finger. This big vein is probably not so infrequent as would appear from the recorded cases, for the vein collapses after death and is not seen unless the falciform ligament is specially examined. I have seen it full of carcinoma in a case of carcinoma with cirrhosis.

As a result of the anastomosis thus opened up the veins of the abdominal wall, especially around the umbilicus, may become dilated and prominent. When marked, this condition is spoken of as a "caput medusæ." It is hardly ever so well developed as the caput medusæ produced by mechanical obstruction of the inferior vena cava. There is a difference in the situation of these two collateral venous circulations in the abdominal wall; that due to portal obstruction is most marked around the umbilicus, while that seen in obstruction of the inferior vena cava runs from the middle of the groins to the costal arches and avoids the umbilicus.

It may be pointed out that in healthy subjects the round ligament at its junction with the right branch of the portal vein is pervious for a distance of ½ to 1½ inches and then becomes occluded. This channel is no doubt utilized in the formation of a collateral and compensatory circulation.

In very rare instances the ductus venosus, which in the fœtus runs directly from the umbilical vein into the inferior vena cava, is persistent, and thus provides a direct communication between the portal vein and the inferior vena cava.

In an interesting case of hepatic cirrhosis with obstruction of the superior vena cava described by Duckworth and Garrod § there were great by dilated veins under the skin of the abdomen, the blood running into them in both directions, but it is noteworthy that there was an absence of these veins around the umbilicus.

In ordinary cirrhosis extensive ascites may so compress the inferior vena cava as to lead to the development of a caput medusæ comparable to that seen when there is obstruction to the passage of blood through the inferior cava. An extremely rare complication of cirrhosis is thrombosis of the inferior vena cava, which would produce the same conditions.

Councilman ‖ has met with a terminal streptococcal infection in cirrhosis in which the retroperitoneal glands and tissues were suppurating and had thus caused thrombosis of the inferior vena cava.

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* Sappey: Mem. de l'Acad. Roy. de Med., xxiii, p. 270.

† Champneys: Journ. Anat. and Physiol., vol. vi, p. 417, 1872.

‡ Wilks: Pathological Anatomy, p. 467, 1889.

§ Duckworth and Garrod: St. Bartholomew's Hosp. Reports, vol. xxxii, p. 71.

‖ Councilman, W. T.: Trans. Assoc. American Physicians, vol. xi, p. 213, 1896.

Occasionally there may be a kind of belt of dilated cutaneous venules over the line of attachment of the diaphragm. This, however, is not pathognomonic of portal obstruction, as has sometimes been thought, but occurs in emphysema, bronchitis, and sometimes in elderly men without at any rate any manifest morbid lesion.

(*b*) At the terminations of the intra-abdominal parts of the alimentary canal: The veins of the œsophagus, which open into the azygos veins, communicate at the cardiac orifice with the gastric veins and so with the portal vein. This communication may become so developed as to produce varicosities at the lower end of the œsophagus, or "œsophageal piles," and from ulceration or rupture may be the source of severe hæmorrhage. Though usually developed to a certain degree, it is only occasionally that there are large varicosities. This may be explained on the ground that there are valves guarding the entrance of the gastric vein (Macalister *), which would tend to prevent reflux of blood from the portal into the gastric veins.

It should be noted that œsophageal varix may occur without any cirrhosis of the liver; cases of fatal hæmorrhage have occurred from this cause in a child and in a boy of seventeen.†

The coronary vein of the stomach communicates with the phrenic vein, and it would be natural to expect to find that the branches of the gastric veins would be often dilated. This is very seldom observed, though it is possible that it is overlooked. The walls of the vein may undergo chronic inflammation, and from the results of fibrotic atrophy local dilatations may result. These become adherent to the mucosa and the raised area may, as the result of traumatism, toxic irritation, or microbic infection, become ulcerated. The resulting hæmorrhage may, as in two cases of cirrhosis recorded by Letulle,‡ be fatal.

Varicosity of the gastric veins and fatal hæmatemesis may occur in the absence of any hepatic disease. (Barr, § Lancaster ‖.)

Dilatation of the anastomosis between the superior hæmorrhoidal vein opening into the inferior mesenteric, on the one hand, and the middle and inferior hæmorrhoidal, which pour their blood into the internal iliac vein, on the other hand, may also occur. It would if excessively developed lead to piles, and from *a priori* reasoning it has been assumed that piles are common in cirrhosis. As a matter of experience, however, this is not the case, and it must be admitted that constipation is a far more frequent and important factor in the production of piles than cirrhosis.

It is possible that the compensatory effects of these anastomotic channels have been somewhat overestimated. Thus the dilated venous channels may be absent in cases of latent cirrhosis dying from other causes, and may be well developed in cases dying with ascites. In the latter instance the compensatory process, though considerable, cannot be regarded as having been successful.

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* Macalister's Anatomy, p. 431.

† Graham: Trans. Assoc. American Physicians, vol. xi, p. 215, 1896.

‡ Letulle: La Presse Médicale, Nov. 29, 1898.

§ Barr: Lancet, 1889, vol. ii, p. 1226.

‖ Lancaster: Trans. Clinical Soc., vol. xxx, p. 32.

In an examination of 78 autopsies of cases with cirrhosis, Sears and Lord[*] found this dilated anastomosis in 29 cases, being most often present when the cirrhotic process was most advanced. But in 22 out of the 29 cases there was ascites.

Bad Effects and Results which may Depend on Excessive Development of this Venous Anastomosis.—The development of a free communication between the portal and general systemic veins, while it relieves portal engorgement, may lead to bad effects. In the first place, if the communications are extensive, it necessarily follows that a considerable quantity of blood carrying the products of digestion will pass directly into the general circulation instead of going through the liver. As a result poisons absorbed from the intestine would not be stopped by the liver, but would pass freely into the general circulation and set up toxæmia. If the anastomosis is very free, the condition would resemble that in Eck's fistula, or the experimental communication between the inferior vena cava and the portal vein, which results in all the portal blood passing into the inferior vena cava. A most elaborate and interesting series of experiments on these lines was carried out by Hahn, Nasse, Nencki, and Pawlow.[†] In animals thus treated, effects equivalent to those of hepatic insufficiency naturally resulted, and if a proteid diet was adopted, symptoms comparable to those of uræmia developed, which were regarded as due to the presence of carbamic acid in the blood. In man excessive development of the collateral circulation may lead to a toxæmic condition verging on uræmia. This has been insisted on by Stockton,[‡] and it is interesting to note that one of Morison's[§] patients, after the operation for the surgical relief of ascites, was alternately excited and depressed for three weeks after the operation. Possibly a very free collateral anastomosis between the portal and general venous systems, while relieving portal engorgement, may lead to arteriosclerosis and granular kidneys. In cases where the two conditions of renal and hepatic fibrosis are combined the patients usually die from renal disease with latency of the hepatic cirrhosis. This was the termination of Jacobson's[‖] remarkable case, where a vein as large as a thumb ran between the portal vein and the left renal vein.

In the second place, hæmorrhage may occur from rupture of the dilated venous anastomoses. This generally occurs into the gastrointestinal tract, but in very rare instances, of which examples will be given, hæmorrhage may take place into the abdominal wall or into the peritoneal cavity. Hæmatemesis not very infrequently results from rupture of an ulcerated varicose vein in the œsophagus, while slight bleeding from piles may go on for a considerable time.

The occurrence of a hæmatoma in the anterior abdominal wall close to the round ligament, though a rare event, is another illustration of a pathological event in the course of this compensatory mechanism, and may be considered as analogous to hæmatemesis from dilated œsophageal veins.

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[*] Sears and Lord: Boston Medical and Surgical Journ., vol. cxlvii, p. 285, Sept. 11, 1902.

[†] Archiv f. experiment. Path. u. Pharmak., Bd. xxxii, S. 161.

[‡] Stockton: Journ. American Med. Association, 1901, p. 817.

[§] Morison: Lancet, 1899, vol. i, p. 1426.

[‖] Jacobson, G.: Archiv. Général. de Méd., 1893, vol. i, p. 353.

A case is recorded by Lefas* of a hæmatoma the size of a tangarine orange to the left of the middle line in a man aged fifty-five with cirrhosis. There is an interesting specimen, 380.8, in the Museum of the College of Medicine, Newcastle-upon-Tyne, showing a large hæmatoma in the abdominal wall close to the round ligament of the liver, which contains a number of dilated veins. The patient, a man aged forty-eight, had been tapped two and one-half years before his death; after this, the ascites did not return. Six months before death he had phlebitis of the right femoral vein, and one month before death he had a sudden attack of abdominal pain and swelling to the left of the umbilicus. Ten days before death he had epileptic fits and died with pleurisy and a pyopneumothorax. The liver showed ordinary portal cirrhosis.

In extremely rare instances traumatism may lead to rupture of dilated veins in peritoneal adhesions and so to extensive hæmorrhage into the peritoneum.

A man aged forty-five received a blow on the abdomen and died in St. George's Hospital after being in a condition of collapse for eleven hours. At the postmortem examination there was cirrhosis of the liver (78 ounces) with marked engorgement of the veins in the substance of the liver, so that the organ had a nævoid appearance. The abdominal cavity was full of blood. The spleen was enlarged, and on section showed hæmorrhage into its substance, but there was no rupture of its capsule. There was laceration of some vascular adhesions, from which the blood probably came. Microscopically the liver showed multilobular cirrhosis of old date with hardly any recent proliferation of the connective tissues. The cirrhosis appeared to be latent.

Hepatic Artery.—The hepatic artery is usually considerably enlarged, as it is thought to supply the added fibrous tissue with blood. Chronic endarteritis is not a special feature of ordinary cirrhosis, but it is seen in cirrhosis due to hæmochromatosis and sometimes in cases of cirrhosis in syphilitic patients and in parasyphilitic cirrhosis.

Condition of the Spleen in Portal Cirrhosis.—The spleen is enlarged in portal cirrhosis, though not so markedly as in hypertrophic biliary cirrhosis.

In 147 cases of cirrhosis examined at St. George's Hospital the average weight of the spleen was 10 ounces. In Kelynack's series of 84 cases of cirrhosis the average weight of the spleen was 12.9 ounces. So that if the weight of the normal spleen be taken as 7 ounces, there is seen to be a very definite increase in cirrhosis. The weight of the spleen varied between the two extremes of 2 ounces, in a case of latent cirrhosis, and 48 ounces, in a man who survived thirty months after the operation for producing artificial peritoneal adhesions had been performed. This weight is very exceptional in portal cirrhosis, though not in hypertrophic biliary cirrhosis.

In cases where there has been fatal and very profuse hæmatemesis or very rapid ascites, the spleen may be small.

In latent cirrhosis the enlargement and increase in the weight of the spleen are much less than in cases where death has been directly due to cirrhosis.

In 74 cases where cirrhosis, though present, was not the cause of death, the average weight of the spleen was 9 ounces; while in 73 cases where death was referred to the effects of cirrhosis, the average weight of the spleen was 11.5 ounces.

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* Lefas: Bull. Soc. Anat. Paris, 1902, p. 586.

The fact that the spleen is bigger and heavier in cases dying from the effects of cirrhosis than in latent cirrhosis may be explained as depending on two factors which come into play in progressive cirrhosis,—viz., (i) general toxæmia, and (ii) increased pressure in the portal vein,—but are either absent or largely obviated in latent compensated cirrhosis.

In very exceptional cases, of which I have seen two, the spleen is greatly enlarged and the liver shows slight and very old fibrosis. One of these cases was published by Dr. R. S. Trevor,* the other was a typical case of chronic splenic anæmia under the care of my colleague, Dr. Ewart. This combination is not Banti's disease, for in that condition cirrhosis supervenes as a terminal phenomenon in the course of chronic splenic anæmia. It appears indeed to be the reverse of Banti's disease, and to be a continuation and exaggeration of morbid changes in the spleen in cases of latent or practically cured cirrhosis.

Morbid Appearances of the Spleen.—The capsule of the spleen is often thickened and shows perisplenitis. This may be local, the thickened area being a lamellar fibroma, a condition frequently seen in splenic enlargement from any cause, or it may be general, and then usually forms part of a general chronic peritonitis.

In 131 cases of cirrhosis analysed by Yeld † perisplenitis was present in 43, or 33 per cent.; and in 23, or 29.5 per cent., of the 78 cases recorded by Sears and Lord.‡

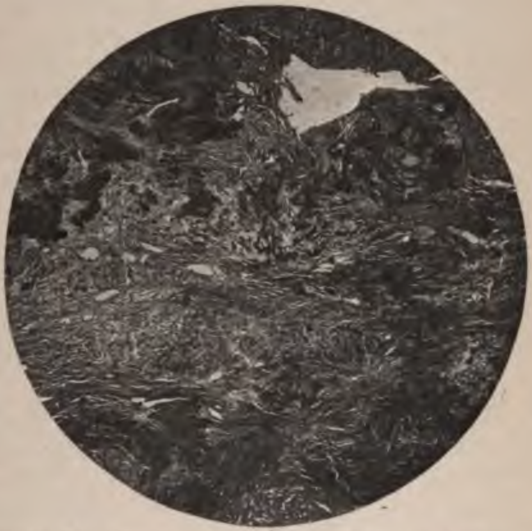

FIG. 34.—PHOTOMICROGRAPH SHOWING FIBROUS AREA IN THE SPLEEN.

Around it are dark masses which stained blue with ferrocyanide of potassium and hydrochloric acid. (By S. G. Penny, Esq.)

The spleen is frequently adherent to the parietal peritoneum of the diaphragm, abdominal wall, stomach, etc. When the spleen and liver are both considerably enlarged, the left lobe of the liver may overlap the spleen. Though this is more likely to occur in hypertrophic biliary cirrhosis, it may occasionally be seen in multilobular cirrhosis.

On section the organ is sometimes firmer than natural and fibrosed; in other cases, probably as the result of terminal infections, it is soft or even diffluent. Occasionally areas of extravasation of blood are seen.

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* Trevor, R. S.: Trans. Path. Soc., vol. liv, p. 302.

† Yeld, R. A.: St. Bartholomew's Hosp. Reports, vol. xxxiv, p. 215.

‡ Sears and Lord: Boston Medical and Surgical Journ., vol. cxlvii, p. 285.

In a case of fatal cirrhosis which survived Morison's operation, for producing artificial peritoneal adhesions, for two and one-half years the spleen was greatly enlarged, weighing 48 ounces, and contained a large number of gritty spots. Microscopically these areas showed fibrosis surrounding calcareous granules and particles which turned blue on being treated with ferrocyanide of potassium and hydrochloric acid. (*Vide photomicrograph.*) There was also considerable hyperplasia of the endothelial cells lining the sinuses.

Microscopic Appearances.—There is dilatation of the blood-vessels generally, which spreads to the capillaries in the Malpighian bodies and is followed by secondary atrophy of the lymphoid tissue in the Malpighian bodies. Some difference of opinion exists as to proliferation of the splenic pulp. Oestreich * described it in early cases, but neither Sieveking † nor Azzurrini ‡ has confirmed this. Fibrosis of the spleen due to increase in the trabeculæ occurs in cases of some standing.

The Cause of Splenic Enlargement in Hepatic Cirrhosis.—There are two views as to the causation of the splenic enlargement.

(I) The mechanical view: that it is due to backward pressure and chronic venous engorgement of the organ brought about by the portal obstruction existing in the liver. In favour of this is the fact that the enlargement may diminish after profuse gastro-intestinal hæmorrhage or diarrhœa. The manifest objection to this theory is that in the chronic venous engorgement of heart disease the spleen, though firmer than natural, is not increased in weight. This is well brought out in a comparison drawn up by Kelynack § between the weights of the spleen (i) in 84 cases of cirrhosis and (ii) in 56 cases of nutmeg liver, in cases of heart disease uncomplicated by any febrile or other conditions likely to affect the size of the organ.

	AVERAGE WEIGHT.		
	Males.	Females.	Both Sexes.
"Hepatic" spleen	14.25	11.62	12.93
"Cardiac" spleen	7.32	7.32	7.32

Some explanation of this difference might be found in the fact that the liver would act as a kind of buffer when the backward pressure is due to heart or lung disease, and so protect the spleen from excessive venous engorgement, whereas in cirrhosis the spleen is nearer to the venous obstruction. In support of this argument of Foxwell's ‖ it may be added that in thrombosis of the splenic vein the spleen is very markedly enlarged. But, on the other hand, the splenic enlargement is much more marked and may precede any manifest change in the liver in hypertrophic biliary cirrhosis,** in which the obstruction to the passage of blood through the liver is, as shown by the slighter fibrosis, much less than in portal cirrhosis. It appears, therefore, that backward pressure does not, at any rate completely, explain the splenic enlargement.

(II) The toxæmic theory: that the spleen is enlarged as a result of poisons circulating in the blood and reaching it through the splenic artery, and that there is an active inflammatory swelling of the spleen like that seen in bacterial and some toxic conditions, such as the early stages of syphilis, Landry's paralysis, and perhaps exophthalmic goitre. In favour of this view is the fact that the spleen is not enlarged in cases of latent cirrhosis, where the disease is arrested or compensated for. The toxæmia responsible for the enlargement might be either the same as that producing hepatic cirrhosis or it might be secondary to hepatic insufficiency, the cirrhotic liver allowing poisons, which should normally be arrested by it, to pass into the general circulation.

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* Oestreich: Virchow's Archiv, Bd. cxlii, S. 285.

† Sieveking: Centralblatt f. allg. Path. u. path. Anat., June, 1894, S. 1017.

‡ Azzurrini: Lo Speriment., An. 56, Fascic. v–vi, p. 597, 1903.

§ Kelynack, T. N.: Birmingham Med. Rev., Feb., 1897.

‖ Foxwell, A.: The Enlarged Cirrhotic Liver, p. 6, 1896.

** Compare F. P. Weber: Edinburgh Med. Journ., Dec., 1897, vol. ii, p. 579.

This question is a difficult one. The spleen and liver react in different degrees to hæmic intoxication, the spleen usually to a greater extent. Probably the spleen may suffer to some extent at the same time as the liver in early cirrhosis, if the poison, reaching the liver, as it generally does, from the portal system escapes into the general circulation. But when the liver becomes unable to stop poisons and general toxæmia supervenes, the conditions favourable for splenic enlargement have become greatly increased.

Histologically Oestreich * found proliferation of the splenic pulp and concluded that it was due to toxines reaching the organ by the splenic artery.

To sum up: Splenic enlargement in cirrhosis probably depends primarily on microbic or other poisons setting up hyperplasia and inflammatory softening of the substance of the organ so that it readily gets overdistended with blood. Though chronic venous engorgement alone is not enough to explain enlargement of the spleen, it favours the stagnation of poisons and irritating bodies, and, further, it supplies blood to distend the softened splenic blood sinuses. Hence it may be concluded that the enlargement of the spleen is primarily due to toxic action and is aided by increased venous pressure in the portal system.

Relation between the Size of the Liver and that of the Spleen.—In hypertrophic biliary cirrhosis the liver and spleen are both very considerably enlarged, and it might be surmised that in portal cirrhosis there would be a general relationship between the size of the liver and that of the spleen. Careful examination of cases and statistics shows that this point is a complicated one, and that no rule can be formulated to the effect that the size of the liver and spleen varies either directly or inversely. Thus, in some cases, especially those running a rapid course and those showing a mixture of portal and biliary cirrhosis, the liver and spleen are both enlarged. On the other hand, in latent or compensated cirrhosis the liver is considerably increased in size, being bigger than in cases fatal from the effects of cirrhosis, while the spleen is either of normal size or but slightly heavier than normal. Again, in cases fatal from cirrhosis the liver is sometimes smaller than natural, while the spleen is almost constantly larger and heavier.

In order to see whether any relationship exists between the weight of the liver and of the spleen in cirrhosis the following percentages were extracted from a number of cases examined at St. George's Hospital.

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* Oestreich: Virchow's Archiv, Bd. cxlii, S. 285.

In 43 male cases in which the liver weighed over 60 ounces (averaging 79.6 ounces) the spleen averaged 11 ounces; while in 7 males in which the liver weighed under 50 ounces (averaging 39.4 ounces), the spleen weighed 9.4 ounces.

In 11 female cases in which the liver weighed over 55 ounces (averaging 73.5 ounces), the spleen weighed 7.6 ounces; while in 9 cases in which the liver weighed less than 45 ounces (averaging 35.4 ounces), the spleen weighed as much as 9.8 ounces.

Therefore, in male cases of cirrhosis, whether fatal from the disease or from other causes, large livers were associated with a more considerable enlargement of the spleen than is seen when the livers are small. But in a corresponding collection of female cases the spleen was heavier in the series of small livers than in the large liver series.

A consideration of the whole subject shows that the weight of the spleen has no constant relation to that of the liver, and that it depends on other factors, which may or may not be associated with increased weight and size of the liver.

Morbid Appearances in other Viscera.—Some writers have spoken of hepatic cirrhosis as a disease which is not strictly limited to the liver. but is part of a general change, and in this respect it might be compared to the condition of red granular kidneys which are a local manifestation of a general vascular change—arteriosclerosis. Portal cirrhosis might in the same way be considered to be part of a general change in the alimentary system, for the spleen, the intestines, and the pancreas commonly show changes in hepatic cirrhosis. Some of the changes are secondary to portal obstruction, but this does not account for the visceral changes, and some of them must be regarded as concomitant effects of a general cause, in many cases alcoholism. As bearing on this conception of cirrhosis as part of a widespread change in the alimentary system, Klippel and Lefas * have pointed out that in some instances of cirrhosis the changes may be more advanced in the pancreas than in the liver. This secondary relationship of cirrhosis to a general cause is also seen in hæmochromatosis, where, as a secondary result, cirrhosis of the liver and pancreatic fibrosis may occur. (*Vide* Pigmented Cirrhosis.)

The Œsophagus.—There may be chronic œsophagitis with general thickening of the mucous membrane, which in places shows localized elevations due to hyperplasia of the epithelium—small corns. The longitudinal veins running in the submucosa of the œsophagus in its lower 3 or 4 inches are often dilated and varicose. (*Vide* Collateral Circulation Between the Portal and General Venous System.) Inflammatory changes in the varicose veins lead to adhesions between the veins and the mucous membrane, and the veins with adherent mucous membrane covering them stand up as elevations on the surface of the œsophagus. Ulceration may then occur and give rise to very profuse hæmorrhage.

Stomach.—Portal obstruction induces chronic venous engorgement of the stomach which nearly always shows signs of chronic gastritis. Mammillation of the mucous membrane and pigmentation, especially near the pylorus, are often present. There is occasionally dilatation of the gastric veins close to the cardiac orifice, but a varicose condition of the veins of the stomach is very rare. Cases of hæmatemesis depending on ruptured varicose gastric veins have been described. (*Vide* p. 212.) Acute gastritis sometimes supervenes on the chronic gastritis and small multiple ulcers which are quite superficial may then occur. The association of a single chronic gastric ulcer with cirrhosis of the liver is, however, rare.

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* Klippel and Lefas: Rev. de Méd., Jan., 1903, p. 23.

The Small Intestine.—There may be signs of chronic enteritis, such as thickening of the mucous membrane with tenacious mucus on its surface. Mere engorgement is not of very much importance after death, inasmuch as it may be largely due to stagnation of venous blood, from a dependent position of the intestinal coils. The mucous membrane may be pigmented from the effects of chronic catarrhal enteritis and venous engorgement. This is often more marked in the duodenum and the upper part of the jejunum than elsewhere. Occasionally the mucous membrane is œdematous. The subperitoneal tissues of the intestine may also be œdematous, either independently of or in association with œdema of the mucous membrane. Dilated venules and submucous hæmorrhages are sometimes seen.

The small and large intestines become diminished in length in severe cases of portal cirrhosis; instead of 25 feet, the small intestine may only measure 15 feet, while the colon may be shortened in a corresponding or even in a greater degree. This fact, originally observed by Bright, has been explained as due to chronic enteritis, to concomitant chronic peritonitis, or to chronic inflammation of the radicles of the portal vein. It is important in that it diminishes the area of the mucous membrane from which absorption can take place. In rare instances the colon may be œdematous.

A little girl aged ten years was admitted under the care of my colleague, Dr. Ewart, with a temperature of 104°, history of diarrhœa, and a swollen abdomen; the next day the abdomen was more distended and it was thought that perforation of a typhoid ulcer might have occurred. Mr. Allingham opened the abdomen and found a clear ascitic effusion and a cirrhotic liver. The patient died the next day. At the autopsy the liver (10 oz.) showed extreme portal cirrhosis of a multilobular type; there was no portal thrombosis. The mucous membrane of the colon was enormously swollen from œdema, and showed a little follicular ulceration. There was no hæmorrhage into the mucosa. There was no tubercle. There was probably an acute infection of the colon, which accounted for the high temperature and the acute œdema of the colon.

The rectum occasionally shows dilated veins, but, contrary to what might be expected from the presence of a communication between the portal system and the general venous system in the hæmorrhoidal veins, piles are rare in cirrhosis. Occasionally there is intense congestion of the rectum with small ulcers which may give rise to hæmorrhage of considerable amount.

The Pancreas.—Changes in the pancreas are extremely frequent in portal cirrhosis.

Steinhaus* found chronic interstitial pancreatitis in 11 out of 12 cases; Klippel and Lefas† in 8 cases of portal cirrhosis.

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* Steinhaus: Deutsch. Archiv f. klin. Med., Bd. lxxiv.

† Klippel and Lefas: Rev. de Méd., Jan., 1903, p. 23.

The pancreas is usually enlarged as a whole, but the tail is relatively more affected than the body and head of the gland. In his first series Lefas* found the weight increased by a third. Microscopically there is chronic interstitial pancreatitis, the fibrosis being either perilobular, intralobular, or partly periacinous, but chiefly intralobular. There are scattered areas of small-cell infiltration. The fibrosis resembles that in the liver. Occasionally there is interlobular œdema present. The gland cells undergo fatty and pigmentary degeneration; but according to Steinhaus, the islands of Langerhans, which play an important part in the production of the internal secretion and in the prevention of diabetes, remain intact. In the cirrhosis of hæmochromatosis, however, which is an exception to this rule, the islands of Langerhans are eventually destroyed, and as a result there is diabetes (*diabète bronzé*). Klippel and Lefas find that there is no relationship between the size and consistency of the pancreas and these changes in the liver, and that in some instances the pancreas shows more advanced change than the liver; they regard the change as due to the same factors as cirrhosis, but independent of, and not secondary to, hepatic cirrhosis.

In a case of latent cirrhosis in a woman aged seventy fatal hæmorrhagic pancreatitis occurred. (Pitt.†)

Kidneys.—In the great majority of cases of portal cirrhosis the kidneys are free from any gross old-standing change, but show hypertrophy in about 50 per cent. of the cases.

In 89 cases of fatal cirrhosis collected by Milian and Bassuet,‡ the kidneys were perfectly normal in 19; in 53, or 59.5 per cent., they were healthy or more or less hypertrophied. Pitt § found that when otherwise healthy the kidneys were enlarged in 50 per cent. of the cases of cirrhosis.

This hypertrophy of the renal substance is a point of some interest as regards its explanation. In some instances the hypertrophy may merely be due to overwork from excessive drinking on the part of the patients. It has been suggested that the hypertrophy is a compensatory process with the object of removing the toxic bodies which, owing to hepatic inadequacy, have flooded the circulation. (Mollard.‖) In some instances enlarged kidneys are fatty or affected with cloudy swelling. The kidneys are arteriosclerotic (granular) in about 22 per cent. of cases dying with cirrhotic livers. In about 5 per cent. of the cases there is tubal nephritis. The relation of renal disease to cirrhosis is referred to again under the heading of associated morbid lesions. (*Vide* p. 223.)

Diaphragm.—In long-standing cases where the abdomen has been for a considerable time distended, the diaphragm may show marked muscular hypertrophy from overwork. It is, however, very seldom observed.

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* Lefas: Archiv. Général. de Méd., May, 1900, p. 539.
† Pitt: Trans. Clinic. Soc., vol. xxxii, p. 80.
‡ Milian and Bassuet: Bull. Soc. Anat. Paris, 1903, p. 337.
§ Pitt: Trans. Path. Soc., vol. xl, p. 349.
‖ Mollard: Lyon Médical, t. xcix, p. 665, 1902.

There was great hypertrophy of the diaphragm in a patient who survived the Morison-Talma operation, performed by my colleague, Mr. G. R. Turner for two and three-quarter years.

ASSOCIATED LESIONS.

Tuberculosis.—Tuberculosis is met with in the bodies of patients with cirrhosis more often than in other non-tuberculous diseases.

Thus in 706 fatal cases of cirrhosis obtained by combining the statistics given by Lancereaux,* Pitt,† St. George's, Kelynack,‡ and Yeld,§ 209, or 28 per cent., presented some evidence of tubercle. Taking the general incidence of tuberculosis in routine postmortem work as 27.5 per cent. (Osler‖), and deducting the large number of cases dying directly from tuberculosis—about 14 per cent.—it is evident that tubercle is more frequent in cirrhosis that in ordinary non-tuberculous diseases.

The reason why tuberculosis more commonly supervenes in cirrhosis than in other non-tuberculous diseases is probably that the same conditions favour the production of cirrhosis and tuberculosis. Alcohol and other poisons which induce cirrhosis diminish the resistance of the body and so dispose to the invasion of tubercle. Although a tuberculous cirrhosis (*vide* p. 191) has been described (Hanot and Gilbert **), there is no reason to think that ordinary cirrhosis is ever due to tuberculosis or to tuberculous peritonitis, and when tuberculosis and cirrhosis are associated, the cirrhosis is, as a rule, the older condition.

Age plays some part in influencing the incidence of tuberculosis in patients with cirrhosis. Thus while it is rare in the somewhat infrequent cases of hepatic cirrhosis in childhood, Pitt's statistics show that alcoholic cirrhosis in patients under forty is accompanied by tuberculosis in two-thirds of the cases. The lungs and the peritoneum are the most frequent sites of tuberculosis in the subjects of cirrhosis. The tubercle may be old, acute, chronic or recrudescent, and not infrequently escapes detection during life.

Pulmonary Tuberculosis.—In patients with cirrhosis pulmonary tuberculosis is the direct cause of death in from 12 (Kelynack) to 14.5 per cent. (Rolleston and Fenton), thus agreeing with the general death incidence from tuberculosis. In cases of cirrhosis, whether fatal from the disease itself or from other diseases (excluding tuberculosis), the lungs are the most frequent site of tuberculous lesions, and are more frequently affected than in persons dying from other diseases.

In 584 cases of cirrhosis obtained by adding together the figures in the statistics of Lancereaux, St. George's, Kelynack, and Yeld, tuberculous lesions were found in the lungs in 132, or 22.6 per cent. On the basis of Heitler's †† estimate that tubercle is present in 5 per cent. of patients dying from diseases other than pulmonary tuberculosis—a low estimate—there is a marked increase in the incidence of tubercle in the lungs.

Tubercle is more often found in the lungs in patients who die from the effects of cirrhosis than in patients who have cirrhosis but die from other causes (excluding tuberculosis).

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* Lancereaux: Traité de Maladies du Foie et du Pancreas, p. 302.

† Pitt, G. N.: Trans. Path. Soc., vol. xl, p. 350.

‡ Kelynack, T. N.: Medical Chronicle, Jan., 1897, p. 262.

§ Yeld, R. A.: St. Bart.'s Hosp. Reports, vol. xxxiv, p. 215.

‖ Osler, W.: Practice of Medicine, p. 270, 4th ed.

** Hanot and Gilbert: Archiv. Général. de Méd., tome clxiv, p. 513.

†† Quoted by Hilton Fagge: Practice of Medicine, vol. i, p. 953, 1886.

In 97 cases of cirrhosis where death was not due to pulmonary tuberculosis tubercles were found in the lungs in 17. Of these 97 cases, 47 were fatal from the direct effects of cirrhosis, and pulmonary tubercle was found in 10, or 21.2 per cent.; while in the remaining 50 cases where cirrhosis was latent and death was due to some independent cause, pulmonary tuberculosis being of course excluded, tubercle was present in 7, or 14 per cent.*

Tuberculous Peritonitis.—The peritoneum is next to the lungs the most frequent situation of tuberculous infection in cirrhosis. In 584 cases of cirrhosis obtained by combining the statistics of Lancereaux, Rolleston and Fenton, Kelynack, and Yeld there were 53 cases of peritoneal tubercle, or 9 per cent. In a large number of cases of peritoneal tubercle the lungs are previously infected. Tuberculous peritonitis is rare in adults; when it does occur in males, it is most often in hepatic cirrhosis. Probably the peritoneum is rendered more susceptible to infection by the chronic portal engorgement and possibly by pre-existing chronic peritonitis of a slight degree. In 121 cases of cirrhosis Kelynack found active tuberculosis of the peritoneum in 12, in 4 of whom the peritoneum was alone affected, thus contravening what is known as Godalier's law, that when there are tubercles on the peritoneum they will also be found in the pleuræ. This strongly suggests that cirrhosis of the liver disposes to the local invasion of the peritoneum by tubercle.

Chronic Peritonitis.—A certain degree of chronic peritonitis is often seen in the bodies of those who have died from cirrhosis of the liver, but a high degree of chronic peritonitis is comparatively rare in association with well-marked cirrhosis.

In Yeld's 131 cases of cirrhosis simple chronic peritonitis was present in 10.7 per cent., and in Sears and Lord's † 78 cases in 19 per cent.

Simple chronic peritonitis may be associated with arteriosclerosis; in common with the other serous membranes this low form of inflammation, or perivisceritis, has been regarded as depending on arteriosclerosis. Alcoholism and venous engorgement have both been regarded as causes of chronic peritonitis. As has just been pointed out, tuberculosis may supervene in the peritoneum, and eventually tuberculous peritonitis may result.

Arteriosclerosis.—From the fact that cirrhosis and arteriosclerosis are met with at about the same time of life, it is natural to find arterial degeneration of a greater or lesser degree in the bodies of patients dying from cirrhosis. There is, however, no direct relationship between these two conditions; cirrhosis is accompanied by a low-tension pulse and thus does not tend to set up arterial degeneration, while endarteritis is not a cause of genuine hepatic cirrhosis. In some exceptional instances marked syphilitic endarteritis is associated with hepatic cirrhosis (probably parasyphilitic) in children, and in the rare disease hæmochromatosis, cirrhosis of the liver and endarteritis of the hepatic artery may occur.

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* Rolleston and Fenton: Birmingham Med. Review, Oct., 1896.

† Sears and Lord: Boston Med. and Surg. Journ., vol. cxlvii, p. 285.

From the statistical point of view, arteriosclerosis is the commonest, and one of the least essential, morbid changes found in the bodies of patients with hepatic cirrhosis.

In 78 cases of cirrhosis tabulated by Sears and Lord, arteriosclerosis was noted in 49 instances; often, however, there was only a small patch in the aorta.

Heart.—The heart is frequently flabby and dilated and the muscular tissue often shows cloudy swelling or fatty degeneration. These degenerative changes are largely due to concomitant alcoholism.

In 114 cases of cirrhosis, obtained by uniting Cheadle's,[*] and Sears and Lord's statistics, there was fatty degeneration in 33, or 28.9 per cent., and myocarditis in 3.

In rare instances infective endocarditis may occur as a complication. Chronic valvulitis is common just in the same way that arteriosclerosis is frequently associated with cirrhosis.

Renal Disease.—The kidneys in fatal cases of cirrhosis are, generally speaking, free from any marked structural change; they often show enlargement from overwork (drinking), chronic venous engorgement from cardiac failure, or some degree of tubal changes, such as fatty degeneration or cloudy swelling, from toxæmia or alcohol. When definite structural change is present, it is usual to find that the kidney is granular from the effects of arteriosclerosis; definite lardaceous disease or tubal nephritis is quite rare. The association of granular kidney with hepatic cirrhosis is intelligibly explained by the fact that the two diseases are common at the same time of life, and are therefore met with together in a certain number of cases. As Dickinson[†] expressed it, though both the liver and kidney are very liable to fibrosis, this change in the two organs respectively is due to different morbid agencies.

In a careful analysis of 78 fatal cases of cirrhosis, Sears and Lord [‡] found chronic nephritis (interstitial or tubular) in 23, or 29.4 per cent., fatty change in 15, and lardaceous change in 2.

In 440 cases of cirrhosis of the liver obtained by adding together figures obtained from statistics of Pitt,[§] Kelynack,[‖] Yeld,[**] Cheadle,[††] and myself [‡‡] there were 110 with distinct fibrosis of the kidneys, or 25 per cent. In some of the cases the renal change was not very marked, and as the average age for death in cirrhosis is over forty-five years, it is probable that in some instances the change in the kidney was senile.

The incidence of marked arteriosclerotic change in the kidneys is lower. Hawkins [§§] and Dickinson both put it at about 15 per cent. As would be naturally expected from the greater frequency of both hepatic

[*] Cheadle, W. B.: Some Cirrhoses of the Liver, p. 47.

[†] Dickinson, W. H.: Med.-Chirurg. Trans., vol. lvi.

[‡] Sears and Lord: Boston Medical and Surgical Journ., vol. cxlvii, p. 285.

[§] Pitt, G. N.: Trans. Path. Soc., vol. xl, p. 348.

[‖] Kelynack, T. N.: Birmingham Med. Review, Feb., 1897.

[**] Yeld, R. A.: St. Bartholomew's Hospital Reports, vol. xxxiv, p. 215.

[††] Cheadle, W. B.: Some Cirrhoses of the Liver, p. 51.

[‡‡] Rolleston and Fenton: Birmingham Med. Review, Oct., 1896.

[§§] Hawkins, H. P.: Allbutt's System, vol. iv, p. 186.

cirrhosis and arteriosclerosis in men, the two conditions are more often seen associated in the male than in the female sex.

The question whether a granular kidney is more often associated with a large or with a small cirrhotic liver has been referred to already (p. 199). Pitt's and my own observations point to a small cirrhotic liver as more frequently associated with a granular kidney; Price's statistics were to the opposite effect.

Cirrhosis Complicated with Carcinoma, etc.—The form of primary carcinoma of the liver described by Hanot and Gilbert as cancer with cirrhosis is essentially cirrhosis first with a secondary hyperplasia of the liver cells. At first this hyperplasia is compensatory and gives rise to cirrhosis with adenoma; subsequently the cellular proliferation becomes so riotous as to be malignant and constitutes carcinoma. It is very hard to draw the line between the different stages of cirrhosis, cirrhosis with adenoma, and carcinoma with cirrhosis. The latter condition is undoubtedly rare, like other forms of primary carcinoma of the liver, but Hanot and Gilbert[*] considered that one-third of the cases of primary carcinoma of the liver were of this nature. A full description of primary carcinoma with cirrhosis will be found on page 473.

Secondary Carcinoma in a Cirrhotic Liver.—Cirrhosis of the liver and carcinoma elsewhere in the body are both so common that at first sight it would appear probable that the occurrence of a secondary growth in a previously cirrhotic liver would not be rare. It must, however, be extremely rare; Hanot and Gilbert[†] refer to its hypothetical existence, but say no more about the subject. I have never seen a case. Hale White[‡] refers to a case of sarcoma of bone with a secondary growth in a cirrhotic liver. Poulain[§] and Achard and Laubray[‖] have described cases secondary to carcinoma of the colon and stomach.

Other Accidental Lesions in the Liver.—In a few cases a hydatid cyst has been found embedded in a cirrhotic liver. (*Vide* Hydatid Disease, p. 395.) Gummata and universal cirrhosis are seldom combined. In 86 cases of hepatic gummata collected by J. L. Allen there was cirrhosis in 4, or 4.6 per cent. (*Vide* p. 356.) Tubercles are sometimes seen implanted in a cirrhotic liver. It is rare to find cirrhosis and lardaceous disease combined. A tight-laced liver may become cirrhotic. This condition is figured on page 10.

CLINICAL COURSE.

The course of ordinary cirrhosis may be divided into: (1) The early or pre-ascitic stage, which is often divided into two by early hæmatemesis. (2) The late or ascitic stage.

Cases may die from intercurrent diseases during the course of cirrhosis or may be cut off by a very profuse gastro-intestinal hæmorrhage long before ascites has developed. Again, complications, such as tuberculosis, cardiac failure, peripheral neuritis, or other manifestations of alcoholism, may supervene and prove fatal or mask the symptoms of cirrhosis.

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[*] Hanot and Gilbert: Études sur les Maladies du foie, p. 13.

[†] Hanot and Gilbert: Études sur les Maladies du foie, p. 13.

[‡] Hale White: Allbutt's System, vol. iv, p. 208.

[§] Poulain: Bull. Soc. Anat. Paris, Dec., 1899.

[‖] Achard and Laubray: Mem. et Bull. Soc. Méd des Hôp. Paris, April 25, 1902, p. 335.

The early stage begins gradually and vaguely; though in some cases it may be dated back to some acute illness or to a passing attack of gastro-enteritis. The symptoms are mainly those of dyspepsia, often of an alcoholic nature, with loss of appetite, occasional nausea and vomiting, especially in the morning, flatulence, abdominal pain or unrest, and looseness or irregularity of the bowels. Sometimes symptoms are absent; at other times they are those of chronic alcoholism. Bodily strength, vigour, and energy may be seriously impaired, and the condition resembles neurasthenia; or, on the other hand, there may be little or no complaint of altered health.

There may be some heaviness or tenderness in the epigastrium and hypochondrium, especially after meals, which is partly due to dyspepsia and perhaps partly to hepatic enlargement. The liver is generally somewhat enlarged and may be slightly tender. The enlargement may vary considerably within short intervals, and is chiefly due to vascular engorgement. The spleen is usually not felt to be enlarged, but it may be palpably enlarged, especially shortly before hæmatemesis supervenes.

Epistaxis may occur now and then, but the most important event in the early stage is the occurrence of hæmatemesis. This may come on after some premonitory discomfort and fever, or may occur with little or no warning, except perhaps slight faintness immediately before a large quantity of blood is brought up. It is only very occasionally fatal and is very seldom repeated within a short interval. After it the patient is blanched and anæmic for a time, but soon recovers.

Usually some months or even years elapse after hæmatemesis before ascites develops, especially if the patient has taken warning and altered his manner of life. The disease may then become latent from the development of compensatory processes. But in cases of acute cirrhosis, where there is fever, the effects of hæmatemesis are hardly recovered from before the abdomen shows signs of ascites.

The Late or Ascitic Stage.—The development of ascites may come on somewhat suddenly; when it occurs quite suddenly and with great rapidity it may be due to another factor, viz., thrombosis of the portal vein. The development of ascites may be preceded by gaseous distension of the intestines, which for a time may mask the presence of ascites. Œdema of the feet may also precede instead of following the appearance of ascites.

When ascites occurs, the patient has undergone a considerable amount of wasting, shows marked muscular debility, and is unfit to be out of bed. The wasting of the temporal and facial muscles gives a characteristic appearance to the patient. The atrophy of the thoracic muscles shows up the bony skeleton of the chest, which appears as a prominent object, like a bird's thorax, and contrasts with the swollen abdomen. The skin becomes dry, harsh, and loses its elasticity, and may show petechiæ, while there may be hæmorrhages from the various mucous membranes and oozing from the gums. The ascites may require tapping once, twice, or even oftener, but in cases of cirrhosis uncomplicated by chronic peritonitis paracentesis is seldom required more than once. The patient emaciates rapidly, loses strength, becomes stupid, drowsy, or even delirious, and dies, sinking down in the bed without any great reaccumulation of fluid in the peritoneal cavity. A patient often goes down-hill very rapidly after paracentesis, not because of the tapping, but from the advanced stage of the disease. Sometimes, in fact, ascites disappears, while the patient becomes more drowsy and uræmic, and passes into what may be spoken of as a post-ascitic stage. The patient may then linger on in a semicomatose condition for some weeks, and die from an acute and terminal infection or gradually from mere weakness.

LATENCY.

Cirrhosis of the liver is not uncommonly latent and gives rise to no symptoms. It may be found in the bodies of persons who have died as the result of accidents or from other diseases. It would be incorrect to say that when a patient dies from some other disease the cirrhosis has necessarily been entirely latent, since patients with cirrhosis rapidly die with pulmonary tuberculosis and are very bad subjects for pneumonia, erysipelas, and other acute infections. The fact, however, that out of 166 consecutive postmortem examinations at St. George's Hospital in which the liver was cirrhotic 86, or just over half, died from other diseases and not directly from cirrhosis, shows how frequently cirrhosis remains latent. It thus differs from universal chronic perihepatitis, which is practically always accompanied by ascites. The latency of portal cirrhosis depends on the compensatory processes, *i. e.*, the collateral circulation between the branches of the portal and general systemic veins, and on hyperplasia of the liver cells. These two compensatory mechanisms are further discussed on page 289 under the heading of "Prognosis."

When cirrhosis becomes latent, the liver is enlarged as the result of compensatory hyperplasia of the liver cells. Hanot and Gilbert * have insisted on the enlarged liver of latent cirrhosis, and speak of it under the title of hypertrophic alcoholic cirrhosis. Cirrhosis is more often latent in men than in woman. This is not merely due to the fact that cirrhosis is commoner in men than in women, for the ratio of women to men is lower among the cases dying independently of cirrhosis than among the cases fatal from the direct effects of cirrhosis.

Thus in 167 cases in which the liver was cirrhotic at the autopsy at St. George's Hospital, 121 were males and 46 females, or a ratio of 5 to 2. Of these, 80 died from the direct effects of cirrhosis, 50 being males and 30 females, a ratio of 5 to 3; while of the 87 who died from other factors independent of cirrhosis, 71 were males and 16 females, a ratio of 4½ to 1.

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* Hanot et Gilbert: Soc. Med. des Hôp., May 23, 1890.

MINOR SIGNS AND SYMPTOMS.

Facial Aspect.—The face may be bloated and show acne rosacea due to dyspepsia, either induced by, or independent of, alcoholism; the area of skin affected involves the nose and the cheeks and roughly corresponds with the common site of lupus erythematosus, the so-called "flush area." The condition of the skin of the face varies; in early cases it may be pale and clear, but often it is sallow, muddy, and dirty-looking. The dirty brown aspect of the skin is sometimes so accentuated as to suggest that the cirrhosis may be a terminal stage of hæmochromatosis. In the more advanced stages of the disease the face is drawn and thin, the eyes deeply set, and the conjunctivæ congested and muddy, or slightly icteric. The wasting of the temporal muscles is often very manifest. The skin of the face often shows clusters of dilated vessels or stigmata; these may be capillary or in some instances arterial, as shown by pulsation and by the character of their bleeding. Hæmorrhage from these stigmata or "spider angiomata" may occur on slight provocation. It is an interesting question why these stigmata should develop in cirrhosis; they cannot be due to increased tension in the portal system. It has been thought that they depend on alcoholism; Bouchard[*] has suggested that, owing to altered internal secretion on the part of the liver, the arteries all over the body undergo a special change resulting in local dilatations or nævi. The lips are usually dry and apt to be fissured; the tongue flabby, furred, or dry, and sometimes tremulous. The gums show a tendency to become spongy and, when hepatic insufficiency has become established, to bleed. The throat is apt to be chronically congested and pharyngitis and laryngitis with their attendant symptoms are frequently seen.

The skin of the body is often dry and harsh with loss of elasticity. Local hæmorrhages may occur as the result of slight or unnoticed traumatism. When cirrhosis is advancing, small nævi may crop up all over the surface of the body, and in exceptional instances may unite to form angiomatous areas of considerable extent. Bouchard[†] records a case where they made their appearance when the disease was advancing and receded when improvement took place. According to Gilbert and Herscher,[‡] nævi composed of capillaries are commoner on the trunk, while arterial nævi are more prone to occur on the hands and face. A zone of dilated capillaries on the chest about the attachment of the diaphragm has no real significance, since it is seen in many men of middle age, especially those with emphysema, who have nothing wrong with their livers.[§] Dilatation of the subcutaneous veins around the umbilicus (cirsomphalos) points to portal obstruction; when well marked, this is spoken of as a "caput medusæ." The collateral circulation around the umbilicus, due to portal obstruction, must be distinguished from dilatation and varicosity of the superior and inferior epigastric veins in obstruction of the inferior vena cava. This latter anastomosis is often developed in a minor degree as the result of ascites pressing on the inferior vena cava.

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[*] Bouchard: Rev. de Méd., Oct., 1902, p. 837.

[†] Bouchard: Rev. de Méd., Oct., 1902, p. 837.

[‡] Gilbert and Herscher: Soc. de biolog., Jan. 31, 1903.

[§] For further information about this "costal fringe" the reader is referred to Solis-Cohen's (Amer. Jour. Med. Sc., vol. cviii, p. 135, 1894) and F. P Weber's (Edinb. Med. Journ., April, 1904, p. 346) papers.

Jaundice.—Jaundice is not a prominent feature in portal cirrhosis, but it is met with at some time in the course of the disease, as shown by statistics, in more than one-third of the cases.

Thus, in 293 cases, obtained by combining the statistics of Fagge,[*] Yeld,[†] and Sears and Lord,[‡] jaundice was recorded in 107, or 36.5 per cent.

The jaundice is usually slight and often transient. It may be merely an incident in the course of the disease, and have passed away before the patient comes under observation with indubitable cirrhosis. It not uncommonly happens that there is slight jaundice with staining of the skin and blood serum, but no bile pigment in the urine. To this condition of subicterus, in which the blood serum contains bile pigment, the name "acholuria jaundice" has been given. (Gilbert and Herscher.[§])

Definite, well-marked jaundice may be catarrhal and due to gastro-duodenal inflammation—an exceedingly common event in alcoholic subjects. It is not infrequent in cases of acute cirrhosis; and is then probably due to inflammation of the small intra-hepatic bile-ducts. In rare instances it is dependent on a gall-stone in the common duct, or terminal and the result of acute and widespread degenerative changes in the liver cells (icterus gravis).

Clubbing of the Fingers.—This condition, spoken of as "hippocratic fingers," which is sometimes seen in long-standing cases of hypertrophic biliary cirrhosis, is so rare in portal cirrhosis that it may practically be regarded as a curiosity.

Bouchard[||] described it in a case in 1890. I have watched it develop in a patient in whom, two and one-half years before, Morison's operation for the relief of ascites had been successfully performed. There was no other obvious cause, such as pulmonary or heart disease. In 74 cases of Marie's hypertrophic osteo-arthropathy collected by Symes-Thompson[**] there was no case of portal cirrhosis.

Debility.—Marked weakness and languor out of proportion to the physical signs are not uncommon; this may be one of the first symptoms and may call for treatment before there are sufficient data for diagnosing cirrhosis, and long before ascites has developed. Muscular weakness and asthenia are usually constant late in the course of the disease and are only natural when the poor state of general nutrition is taken into account. The explanation of the debility is partly this and partly a toxæmic state of the blood due to hepatic inadequacy.

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[*] C. Hilton Fagge and Pye-Smith: Practice of Medicine, vol. ii, p. 270, 1886.

[†] Yeld: St. Bartholomew's Hosp. Reports, vol. xxxiv, p. 215.

[‡] Sears and Lord: Boston Medical and Surgical Journ., vol. cxlvii, p. 285.

[§] Gilbert and Herscher: La Presse Médicale; July 29, 1903, p. 541.

[||] Bouchard: Quoted by Klippel and Vigouroux, La Presse Médicale, March 21, 1903.

[**] Symes-Thompson, H. E.: Medico-Chirurg. Trans., vol. lxxxvii

Wasting.—In patients with advanced cirrhosis there is usually very considerable wasting; the muscles of the trunk, extremities, and face become flabby and atrophy. The ribs often show up prominently and the wasted thorax contrasts with the abdomen distended from ascites. The limbs become like spindles. The face gets sharpened, the fat disappears from the buccal pads, and the temporal fossæ fall in, so that the face often has the aspect of a case of advanced pulmonary tuberculosis or of malignant disease. In latent cirrhosis, however, bodily nutrition may be very good, and there may be a thick layer of fat over the body.

I have several times seen somewhat fat patients with latent hepatic cirrhosis die from rapid or generalized tuberculosis. In such cases the existence of cirrhosis is very likely to be overlooked. The large size of the liver is, however, a fairly constant feature of such cases.

Offensive Breath.—In some, but certainly not in all, patients with cirrhosis the breath is very offensive without any local cause, such as decayed teeth, chronic follicular tonsillitis, or ozæna. The odour is often peculiar and is described as cadaveric or earthy. It resembles the smell of dried and decomposing blood and is sometimes associated with oozing from the gums or epistaxis. It is probably due to failure of the antitoxic function of the liver and to the passage into the general circulation of poisons manufactured in the alimentary canal. In other words it depends on hepatic inadequacy, and is therefore of bad omen.

Experimentally Roger and Garnier * find that in healthy rabbits a hypodermic injection of sulphuretted hydrogen is followed by excretion of the gas by the lungs, but that about double the quantity has to be injected into the rectum before it passes through the lungs. When the functional activity of the rabbit's liver has been reduced by the subcutaneous injection of phosphorated oil, a much smaller rectal injection of sulphuretted hydrogen was followed by the excretion of the gas by the lungs.

Saliva.—The amylolytic power of the saliva is not necessarily reduced; it may even be increased. (Robertson.†) If there is ascites or diarrhœa, the amount of saliva will tend to be diminished.

v. Leube ‡ mentions a case of excessive salivation where as much as 3 litres was secreted in one twenty-four hours, and as a result ascites, which was present, disappeared. Cirrhosis of the liver was found after death.

Dyspepsia.—Dyspepsia is almost constant in cases of portal cirrhosis, and usually precedes, often for some years, the first striking manifestation of the disease, namely, hæmatemesis. It may be irritative and intermittent, or flatulent and very persistent. In the early stages it is due to gastritis—often of alcoholic origin—and has a causal relationship to dyspeptic cirrhosis, inasmuch as the chronic gastric catarrh manufactures the toxines which are carried to the liver and induce cirrhosis. Later, when portal obstruction and engorgement of the stomach and intestines have come on, gastritis and indigestion are aggravated. The portal obstruction disposes to infection and at the same time interferes with the digestion and absorption of food. Absorption is also impaired as the result of the curtailed length of the intestinal tract (*vide* Morbid Anatomy), while the process of digestion is interfered with from a deficiency in the secretion of hydrochloric acid. There is loss of appetite for solid food, especially for meat. Morning vomiting may be present and is naturally more often seen in alcoholic subjects. Occasionally acute or subacute attacks of gastritis may supervene, and if seen for the first time in one of these exacerbations, the underlying condition of cirrhosis may not at first be manifest.

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* Roger et Garnier: Soc. de biolog., 1898, p. 714.

† Robertson, W. G. A.: Journ. Path. and Bacteriol., vol. vii, p. 118.

‡ v. Leube: Deutsche Archiv f. klin. Med., Bd. lxvi, 1899.

Diarrhœa.—Comparatively early in the disease diarrhœa or excessive looseness of the bowels may be due to a general catarrhal condition of the intestinal tract in alcoholic subjects, and to diminished and delayed absorption. In other cases diarrhœa may alternate with the more usual state of constipation. Diarrhœa is more often met with in multilobular cirrhosis in children.

In the last stage of the disease, when the patient is in a toxæmic state, diarrhœa may set in and be very rebellious. It may continue until the patient dies of exhaustion. It is, however, possible that the diarrhœa is, like that of renal disease, of use in getting rid of toxic substances.

Constipation.—A sluggish condition of the bowels and constipation are often present. Chronic catarrh of a certain degree may cause it instead of diarrhœa, by impairing the peristaltic powers of the intestine while chronic portal engorgement impairs both the muscular and nervous activity of the bowel. In the later stages the development of ascites tends to produce constipation, both by weakening the muscular walls of the abdomen and by withdrawing water from the bowel. Thus a patient with ascites may present himself chiefly complaining of constipation. Moreover, the milk diet on which a patient with cirrhosis is placed leaves little residue for the fæces and may thus accentuate this tendency. Constipation is an evil, inasmuch as stagnation of food residues in the bowel leads to putrefaction and fermentation and so to autointoxication.

The Urine.—The urine is usually diminished in amount in advanced stages of cirrhosis. The smaller quantity is closely associated with, in fact mainly depends on, low arterial tension, which in turn is correlated with increased blood-pressure in the portal vein. Normally more water passes through the kidneys during digestion, owing to increased absorption from the alimentary canal; in cirrhosis, absorption is delayed on account of the increased venous pressure in the portal vein, and, as a result, the normal relation between the amount of urine excreted during digestion and in the intervals is reversed, more urine being excreted during fasting. This phenomena, described by Gilbert and Lereboullet,* has been termed "opsiuria."

Another abnormal character in the excretion of urine in cirrhosis, described by Chauffard and Castaigne,† is that methylene-blue when taken by the mouth is excreted intermittently, and not continuously, as in health.

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* Gilbert et Lereboullet: Soc. de biolog., March 9, 1901, p. 276.

† Chauffard et Castaigne: Soc. de biolog., 1898, p. 359.

The urine is strongly acid, usually of a high specific gravity, high coloured, often reddish orange, and, like the urine of cardiac disease, commonly precipitates urates on standing.

The amount of urobilin is increased in cirrhosis,[*] while the pigment described as urohæmatoporphyrin, which is in reality not a definite chemical compound, but a mixture of a large quantity of hæmatoporphyrin with a small quantity of urobilin, has been said to occur in the urine of some cases of cirrhosis (McMunn[†]). Indican may also appear in the urine without any evidence of special intestinal disturbance.

Since jaundice is somewhat uncommon in portal cirrhosis, bile pigment is not often found in the urine, but it may be present without any manifest pigmentation of the skin. I have seen this during the comatose condition preceding death. The converse is more often seen, viz., slight icteric colouration of the skin, due to small quantities of bile pigment in the blood serum, without any bile pigment in the urine, though the amount of urobilin in the urine is increased. Gilbert and Herscher,[‡] who call this condition acholuric jaundice, believe that bilirubin is transformed by the kidneys into urobilin. This condition was formerly called "urobilin jaundice."

In cases of advanced cirrhosis a port-wine colouration is, in rare instances, obtained when liquor ferri perchloridi is added to the urine, in the absence of drugs, such as salicylates, salol, diuretin, which give a similar colour reaction; this is due to the presence of diacetic acid (Gerhardt's reaction).

If the urine is previously heated, the colouration is less marked; this is due to the diacetic acid being transformed into acetone, which does not give this colouration with ferric chloride, although it is commonly spoken of as the acetone reaction. The presence of diacetic acid points to the presence in the blood of organic acids, such as oxybutyric acid, or to an acid intoxication (acidosis). This condition is one of great gravity, inasmuch as it may pass into coma. When the urine gives the reaction for diacetic acid, bicarbonate of soda should be given in large doses, and if coma begins to appear, transfusion of saline solution with bicarbonate of soda (2 drams to the pint) should be performed. As is well known, starvation, especially in women with gastric ulcer, may induce diaceturia without any other sign of acidosis.[§]

When the disease is well established, the amount of *urea* excreted is diminished, while that of uric acid is increased. The diminution in the output of urea accompanies, but is not a direct result of, destruction of the liver cells; it is correlated with an increase in the nitrogen excreted in the form of ammonia in the urine. The nitrogen in the form of ammonia may be present in the urine in the normal amount (2 to 5 per cent. of the total nitrogen), but when destructive changes in the liver cells are active, it may rise to as much as 20 per cent. of the total nitrogen. This increase in ammonia is correlated with a diminished formation of urea. According to Herter,[‖] the increase in ammonia is not due to inability of the liver cells to form urea,—for, as shown by Weintraud, if ammonia is given to such patients it appears in the urine as urea,—but to the fact that the ammonia is seized upon by organic acids, such as lactic, before it can be transformed into urea. The ammonia neutralizes the organic acid and so tends to prevent an acid intoxication. In cases where there is extensive destruction of the liver cells leucin and tyrosin may be found in the urine.

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[*] Garrod: Lancet, 1900, vol. ii, Bradshaw lecture. Durandeau: Thèse de Paris, 1900, No. 346.

[†] McMunn: Journal of Physiology, vol. x, 1889.

[‡] Gilbert and Herscher: La Presse Médicale, Dec. 27, 1902; July 29, 1903, p. 541.

[§] *Vide* Rolleston and Tebbs, Brit. Med. Jour., 1904, vol. ii, p. 114.

[‖] Herter, C. A.: Lectures on Chemical Pathology, p. 347.

The *chlorides* are diminished when there is ascites.

Albuminuria is comparatively rare in cases of cirrhosis. When it does occur, it is usually due to some concomitant organic renal disease, such as granular kidney, tubal nephritis, or lardaceous change. In 89 cases tabulated by Milian and Bassuet[*] albuminuria occurred in three. Statistics vary with regard to the association of granular kidneys with a large or with a small liver, and the point cannot be considered settled whether a small or a large cirrhotic liver is most often associated with arteriosclerotic kidneys; my own experience is rather in favour of the small livers being more often seen with granular kidneys.

As a result of hepatic insufficiency a toxæmic state commonly occurs in the late stages of cirrhosis. Sometimes this toxæmia so affects the renal tubules as to give rise to albuminuria and casts in the urine. Albuminuria is sometimes associated with cardiac failure, and it is probable that a toxæmic blood state combined with chronic venous engorgement of the kidney are the most favourable conditions for the production of albuminuria. In rare cases albuminuria may be mechanical and due to the pressure of a considerably enlarged spleen on the left renal vein and possibly on the left kidney. Falkenheim[†] in 1884, and in 1902 the writer,[‡] have observed that intermittent albuminuria may be due to this cause in cases of cirrhosis. In these cases there is considerable albuminuria with high-coloured and lithatic urine, thus resembling that of chronic venous engorgement, when the patient lies on the left side or on his back; while when the patient is in the erect position, lies on the right side or on his face, the urine is free from albumin (Falkenheim).

Albumose is very occasionally observed in the urine when hepatic inadequacy has supervened and may be associated with albuminuria. (Teissier.[§])

It is distinctly rare to find blood in the urine; it may be due to concomitant attacks of subacute nephritis in an already damaged kidney, or it may be due to toxæmia and occur at the same time as epistaxis and oozing from the gums.

Glycosuria.—It is rare to find sugar in the urine in ordinary cirrhosis. Glycosuria occurs in a high proportion of the cases of pigmented cirrhosis from hæmochromatosis (*diabète bronzé; vide* "Pigmented Cirrhosis," p. 300), but it is then due to a concomitant fibrosis of a very intimate nature in the pancreas (involving the islands of Langerhans)—a change which is not present in ordinary cirrhosis. The great rarity of glycosuria in cirrhosis is certainly curious, since the liver is usually regarded as stopping sugar reaching it from the alimentary canal. It might naturally be expected that sugar would pass through the cirrhotic and altered liver, or that by means of the compensatory venous anastomoses some sugar would avoid the liver altogether, and pass into the general circulation and so appear in the urine. Brault's [*] histological examinations of cirrhotic livers show that the glycogenic function of the liver is well maintained, and agree with the clinical fact that glycosuria is very rare. It has sometimes been observed that if an excessive amount of sugar in the form of syrup is given to a patient with cirrhosis, alimentary glycosuria is produced when it would not occur in a healthy person. (Roger.[†])

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[*] Milian and Bassuet: Bull. Soc. Anat. Paris, 1903, p. 337.

[†] Falkenheim: Deutsch. Archiv f. klin. Medicin, Bd. xxxv, S. 446, 1884.

[‡] Rolleston: Lancet, 1902, vol. i, p. 585.

[§] Teissier: La Sem. Méd., 1899, p. 282.

In a normal person 3 ounces (100 grams) of sugar given in half a pint of water or tea on an empty stomach will not produce alimentary glycosuria. To test for alimentary glycosuria this quantity of sugar should be given before food and the urine should be obtained after six hours and tested for sugar. (Von Noorden.[‡])

Alimentary glycosuria is by no means constant in cirrhosis, and even if it were more frequent it would not necessarily show that the liver was at fault; for it appears from Steinhaus' [§] work that it is to be correlated with well-marked changes in the pancreas. The majority of observers, such as Krause and Ludwig,[‖] Bloch,[**] Colasanti,[††] Linoissier and Roque,[‡‡] Gorget,[§§] Strauss,[‖‖] and Ingelnans and Dehon,[***] have come to the conclusion that alimentary glycosuria is a most unreliable sign of hepatic insufficiency. The glycogenic function may be retained while other functions have failed, as is commonly seen in cirrhosis; again, sugar taken into the alimentary canal may be delayed in absorption and undergo fermentation, thus vitiating the test.

Urotoxic Coëfficient.—In cases where hepatic insufficiency is present and due to destructive changes in the liver cells, the toxicity of the urine has been found to be increased (Sourmont,[†††] Gorget [‡‡‡]), as shown by the fact that when injected into dogs it appeared to be decidedly more toxic than healthy urine (Roger[§§§]).

Symptoms Connected with the Vascular System.—From a flabby, possibly fatty, condition of the myocardium the left ventricle may be dilated and a systolic apex murmur and accentuated second sound over the pulmonary artery, due to mitral regurgitation, may be present.

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[*] Brault: Archiv de Méd. expériment. et d'anat. path., tome xiv, p. 453, 1902.

[†] Roger: Rev. de Méd., 1886.

[‡] Von Noorden: XXth Century Practice, 1903.

[§] Steinhaus: Deutsch. Archiv f. klin. Med., Bd. lxxiv, S. 537.

[‖] Krause and Ludwig: Wien. klin. Wochens., 1891.

[**] Bloch: Zeitschrift f. klin. Med., Bd. xxii, 1893.

[††] Colasanti: Archiv. Ital. de Biolog., t. xvii.

[‡‡] Linoissier and Roque: Archiv de Méd. expériment. et d'anat. path., 1895, p. 228.

[§§] Gorget: Rev. de Méd., 1897, p, 545.

[‖‖] Strauss: Berlin. klin. Wochens., May 2, 9, 1898.

[***] Ingelnans and Dehon: Archiv de Méd. expériment. et d'anat. path., t. xv p. 189, 1903.

[†††] Sourmont: Archiv Génér. de Méd., 1892.

[‡‡‡] Gorget: Rev. de Méd., 1897, p. 546.

[§§§] Roger: La Presse Méd., June 26, 1897

When the heart is displaced upwards by ascites, the apex-beat may be found in the fourth or even in the third left intercostal space, and from slight kinking of the pulmonary artery a systolic murmur may be produced in that area. The murmurs at the apex and over the pulmonary artery may disappear after paracentesis of the abdomen. The impulse is, as a rule, feeble. The second sound over the aorta is rather less distinct than in health and is correlated with the low arterial blood-pressure.

The following is a good example of gradual cardiac failure occurring in the course of cirrhosis.

A man aged fifty-six who died under my care in St. George's Hospital had general œdema, slight jaundice, albuminuria, a low-tension pulse, and wandering delirium. He had in previous years had jaundice and hæmatemesis. His respirations were very rapid (56); he had signs of a small pleural effusion on the right side and hæmoptysis. The autopsy showed marked multilobular cirrhosis, kidneys free from old disease, right pleural effusion, collapse of lower lobe of right lung, but no pulmonary apoplexy or tubercle. The heart, 21 ounces, was dilated and hypertrophied and showed fatty degeneration in both ventricles. The valves were healthy. There were several milk spots on the surface of the heart which probably accounted for a soft double murmur heard during life at the bottom of the sternum.

Fatty degeneration of the heart may account for sudden death in cases of cirrhosis.

The pulse-rate is usually slightly quickened; in the late stages when there is a general toxæmic condition the pulse may be rapid and in coma there may be tachycardia. The tension is rather low when the disease is active or producing symptoms, but when it is latent or compensated for it may be normal. After paracentesis the tension of the pulse is lowered; according to Gilbert and his pupils,* this is a mechanical effect due to the increased portal engorgement. It would, however, appear highly probable that the low tension is a toxic effect. The low tension pulse is associated with an increased rate of the pulse and with a small output of urine. Capillary pulsation with perfectly healthy aortic valves has been observed (Bouchard†); and pulsation of the veins of the forearm (Hitschmann ‡) has been recorded.

The Blood.—In early or latent cases when the general health is well maintained the blood is practically normal. When definite symptoms appear there is usually a secondary anæmia which becomes more marked as the disease progresses. From repeated hæmorrhages a grave secondary anæmia with normoblasts may be produced.

In a case quoted by Cabot § the blood count was as low as 1,300,000 red and 22 per cent. of hæmoglobin. v. Limbeck ‖ refers to a case in which the red blood-corpuscles were reduced to 1,500,000.

Occasionally a grave anæmia develops in patients with cirrhosis without any manifest cause, such as hæmorrhage. A distinction should be drawn between secondary and other forms of anæmia developing in patients with cirrhosis, and cases of chronic splenic anæmia in which cirrhosis subsequently develops. To this condition the term Banti's disease has been applied, and it has been thought that the cirrhosis is due to poisons manufactured in the spleen (Chauffard [*]).

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* Gilbert et Garnier: Soc. biolog., Jan. 28, 1899. Gilbert et Weill: Soc. biolog., 1899. DeBrynine: Thèse de Paris, 1900.

† Bouchard: Rev. de Méd., Oct., 1902, p. 837.

‡ Centralbl. f. inn. Med., 1904, S. 42, Jan. 16.

§ Cabot: Examination of the Blood, p. 248, 1897.

‖ v. Limbeck: Pathology of the Blood, p. 318. Transl. in New Sydenham Soc., by Latham and Nachbar.

Secondary anæmia may be modified by cyanosis which leads to an increase in the number of red cells, hence if cyanosis is due to ascites the blood count may be lowered by tapping; on the other hand, rapid ascitic exudation may by concentration increase the blood count; thus tapping, by favouring the recurrence of ascites, has been observed to be followed by a higher blood count. Hence a patient who is manifestly pale and anæmic may have a relatively high corpuscular count. Leucocytosis does not occur except from some complication, such as hæmorrhage or inflammation. The blood serum, as shown by Garrod's test, may appear to contain uric acid. In advanced cases the alkalinity may be diminished from acid intoxication.

Respiration.—When there is abdominal distension from ascites or flatulence, the upward displacement of the diaphragm leads to shallow and more rapid respirations. Apart from this there is nothing noticeable about respiration, as a rule. The respiration rate may be slowed from a toxæmic state of the nerve centres.

The Temperature.—As a general rule, the temperature is not raised; fever is much less frequent in multilobular cirrhosis than in hypertrophic biliary cirrhosis, and when it is met with should at once suggest the presence of some complication, such as tuberculosis, pleural effusion especially on the right side, malaria, infective endocarditis, or other infections.

In 44 cases tabulated by Carrington[†] the temperature was irregular in 18.

Fever is usually associated with hepatic enlargement and sometimes with diarrhœa. It may, in fact, depend on gastro-enteritis, and may then simulate enteric fever or hepatic suppuration. (*Vide* case on page 219.) Apart from manifest secondary infections a febrile temperature is more often seen early in the disease, when its progress is somewhat rapid. Fever is seen in the acute forms of multilobular cirrhosis, and therefore makes the prognosis worse. It may be difficult to decide whether fever in any given case is due to some undetected complication, such as tuberculosis, or whether it depends on acute progressive changes in the liver.

In the case of a man aged forty-one, whose chart is attached, admitted for hæmatemesis, the temperature was almost constantly raised, and in a few weeks ascites developed; it appeared to be a case of acute cirrhosis. Mr. G. R. Turner performed the operation of fixing the omentum between the diaphragm and the liver, and the man greatly improved, the temperature fell, and he went out of the hospital.[‡] He died from cirrhosis in a uræmic state about two and three-quarter years later.

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[*] Chauffard: La Sem. Méd., p. 177, 1899.

[†] Carrington: Guy's Hospital Reports, Series iii, vol. xxvii, 1884.

[‡] *Vide* Rolleston and Turner: Lancet, 1899, vol. ii, p. 1660.

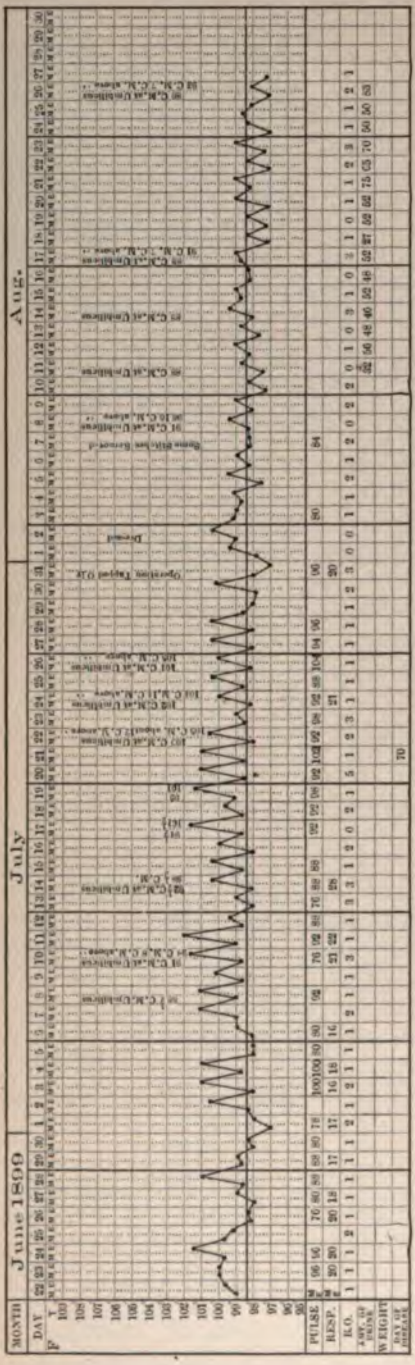

FIG. 35.—TEMPERATURE CHART FROM A CASE OF CIRRHOSIS WITH FEVER, REFERRED TO IN THE TEXT.

Liver.—Clinically the liver is more often enlarged than diminished in size. This point has been specially insisted on by Foxwell,* who considers that "in the large majority of cases of hepatic cirrhosis at all stages of the disease the liver is felt below the ribs." It has often been assumed that enlargement of a cirrhotic liver depends largely on fat, and that this is more likely to occur in beer drinkers than in spirit consumers. But Foxwell's and my own statistics do not bear out the suggestion that cirrhotic livers of beer drinkers are usually larger than those of spirit drinkers. Further, it is far from being universally true that large cirrhotic livers are fatty.

In a decided minority but still in a certain number of cases, chiefly, I believe, in persons whose history shows no alcoholic excess, the liver is considerably smaller than natural. From ascites, flatulent distension, or from obesity it may be impossible to make out the enlargement. Tympanites often precedes and masks the onset of ascites and prevents an accurate estimation of the size of the liver. Before ascites has appeared the liver may usually be felt, sometimes several finger-breadths, beyond the costal margin in the right nipple line, its surface being firm, slightly irregular, and often tender. In other instances its rough and hard margin can be reached by pushing the fingers under the costal margin, while in other cases, although conditions are favourable, the liver cannot be felt on deep inspiration, and percussion may show that there is definite diminution in the liver dulness. It should be remembered that percussion is subject to the fallacy that a resonant note may be obtained over the edge of the liver from distended bowel immediately behind. In rare cases the colon may pass in front of the liver and lead to great diminution in the apparent size of the organ. Palpation is therefore more reliable than percussion.

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* Foxwell, A.: The Enlarged Cirrhotic Liver, p. 20, 1896.

It has been widely assumed that the liver is enlarged in the early stages of the disease and that subsequently it becomes smaller from shrinking and contraction of the fibrous tissue inside it. This sequence of events is sometimes noted (Taylor*); thus a considerable time before death the organ has been found to be large, while at the postmortem some months later it has receded behind the costal arch. At the same time, it is by no means certain that alterations in size of the organ can be referred solely to the contraction of the added connective tissue; for, in the early stage, the enlargement may vary within a comparatively short space of time, thus showing that the increase in size is due to engorgement. Thus, in alcoholic subjects a drinking bout may lead to rapid increase in size of a cirrhotic liver, the organ feeling firm and being tender, while low diet, total abstinence, and judicious purgation are followed by a return to its former size. Dilatation of the heart due to alcoholic excess, or cardiac failure induced in other ways, may give rise to considerable increase in the size of a cirrhotic liver.

It has been noticed by many observers that the cirrhotic livers of people dying from accident and other causes unconnected with the disease are larger than those of patients dying from the disease.† This might be thought to support the view that the liver is enlarged in the early stage from proliferation of the interstitial connective tissue and that later it becomes smaller from cicatricial contraction. But it is more probable that these cases of cirrhosis were latent and that the large size of the livers depended on compensatory hyperplasia of the liver cells, than that the cases were in an early stage of progressive cirrhosis. The surface of the liver may be fairly smooth, especially when it is considerably enlarged, but in other cases its surface is irregular, and sometimes the knobby feel of the "hobnails" is perceptible. These hobnails are not depressed in the centre or umbilicated, but the depressed area of liver substance between two adjacent elevations may imitate the umbilications of multiple carcinomatous nodules.

Hepatic Pain.—Some discomfort and a sense of uneasiness in the region of the liver are very common. Pain is very seldom a prominent symptom, but nevertheless it is present from time to time in a considerable number of the cases, and may be due to transient attacks of perihepatitis, as shown by the frequency of adhesions between the liver and the diaphragm. Pain of a somewhat severe character over the liver may be due to right-sided pleurisy. Tenderness over the liver is by no means constant; it is often present over large cirrhotic livers after bouts of alcoholic excess, and may be an expression of passive engorgement from failing heart.

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* Taylor, F.: Guy's Hosp. Reports, vol. xlv, p. 310.

† Fagge, C. Hilton: Guy's Hospital Reports, Series iii, vol. xx. Price, J. A. P.: Series iii, vol. xxvii.

Venous Bruits.—In rare instances a venous hum may be heard over the epigastrium which is louder on inspiration. It has been explained as the result of the compensatory dilatation of the venous communications between the portal and the general systemic veins.* The thin-walled and dilated veins may readily be kinked as the result of adhesions or temporarily distorted by the descent of the diaphragm or even by the pressure of a wooden stethoscope.

In a man aged forty-three who was under my care in St. George's Hospital there was a continuous bruit in the epigastrium resembling the *bruit de diable* in the neck. At the autopsy the liver was markedly cirrhotic and the round ligament contained a thin-walled vein as large as the little finger. (*Vide* Fig. 32.)

It has also been thought to be due to pressure on the portal vein by enlarged glands, or even to narrowing of the inferior vena cava where it lies in contact with the posterior border of the liver. (v. Gambarati.†)

Spleen.—Enlargement of the spleen is an important feature in portal cirrhosis; it has been shown (p. 214) that the spleen is almost constantly enlarged in fatal cases of progressive cirrhosis, though not to such a marked degree as in hypertrophic biliary cirrhosis. The amount of splenic enlargement has been regarded as an index of the severity of the cirrhosis, and enlargement in cases where the cirrhosis appears to be latent or compensated for should always be an indication for careful treatment and a cautious prognosis. Considerable enlargement may precede hæmatemesis, and its detection may therefore be regarded as a danger-signal and call for free purgation. In some cases of portal cirrhosis enlargement of the spleen is easily made out and the organ can be felt to be firm and resistant. In other instances the splenic dulness is increased, though the organ cannot be felt, while in a number of cases the enlargement of the spleen is obscured by tympanites or ascites. Slight pain or discomfort are sometimes experienced in the splenic region, and, apart from the referred pain of flatulent dyspepsia, may be due to inflammation of the capsule, to tension and engorgement of the spleen, or to dragging on adhesions between the spleen and neighbouring parts.

Venous Bruits.—As in splenic enlargement from other causes, such as malaria, splenic anæmia, etc., a venous bruit, like the well-known *bruit de diable* in the neck of anæmic patients, is occasionally heard over the spleen in cirrhosis. It has also been compared to the uterine souffle. It may be continuous and increased during inspiration, or may only be heard during inspiration. Its position may vary, but is generally in the anterior axillary line. It may be due to temporary or prolonged kinking of the dilated splenic vein or of its branches in the hilum of the spleen.

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* Taylor, F.: Guy's Hosp. Reports, vol. lii, p. 58.

† v. Gambarati: Riforma Med., Feb. 11, 1903, p. 153.

It has also been thought to be due to pressure on the inferior vena cava. (Martini.*)

Œdema of the Feet.—Œdema of the feet usually occurs after, but it may be quite independent of, the development of ascites; it may even come on in the latest stages, when ascites has passed away and the patient is in a toxæmic state. On the other hand, œdema may begin in the feet before the appearance of ascites. The amount of œdema is usually small; sometimes it is very soft, probably from laxity of the skin and underlying tissues from wasting of the subcutaneous fat and of the muscles.

Œdema of the feet is often referred to the ascites mechanically impeding the return of blood through the inferior vena cava. But this explanation will not fit all cases, for example, those in which œdema comes on before the advent of ascites, or when there is so little peritoneal effusion that there can be no increased intra-abdominal tension. In such cases the toxic origin of œdema may be invoked; it has been suggested that there is a poison with a lymphagogue action present in the blood, and that the œdema resembles that of renal disease (Hale White †).

It has been thought that the pressure of a firm cirrhotic liver on the inferior vena cava just before it passes through the diaphragm may be sufficient to give rise to œdema of the feet. This is conceivable, but if it is a factor of any importance, much more œdema of the legs than actually occurs would be expected in cases of malignant disease involving the liver, while a dilated venous plexus, like that seen in mechanical obstruction of the inferior vena cava, should also be present under the skin of the abdominal wall to provide for the return of blood from the lower limbs. As a matter of fact, dilatation of the epigastric and mammary veins may occur when there is ascites, but hardly ever when œdema of the feet is present in the absence of ascites.

In some cases of cirrhosis œdema of the feet may be the outcome of complications, such as the backward pressure of cardiac failure; thus, it may depend on alcoholic dilatation of the heart or on concomitant valvular disease. Again, it may be due to alcoholic neuritis; in the latter contingency there will be muscular tenderness and absence of the knee-jerks. It is probable that a slight degree of peripheral neuritis is more frequent in the course of cirrhosis than is generally recognized, and that it is specially likely to accompany an aggravation of the liver symptoms with abdominal pain, tympanites, and dyspepsia. When œdema of the feet occurs in association with a considerable degree of ascites, it is possible that it is brought about by the pressure of the fluid on the inferior vena cava and the lymphatic vessels going to the thoracic duct.

General œdema is very rare, but the dropsical condition of the legs and thighs may pass up onto the abdomen and appear as a lumbar cushion on the back.

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* Martini: Brit. Med. Journ., 1893, vol. ii. Leudet: Rev. de Méd., 1890, p. 868.

† Hale White: Clinical Journal, April 26, 1899.

McCall Anderson* recorded a case of recurrent attacks of universal dropsy in a boy aged eighteen who had no renal disease and whose liver (4 pounds) showed changes compatible with the view that there was subacute cirrhosis.

ASCITES.

Derivation.—ἀσκός "a wineskin." ἡ ἀσκίτης νόσος, "the wine-skin disease," meaning that disease in which the abdomen looks like a tense wineskin.

The words "ascites," "tympanites," have a feminine adjectival termination, *-ites*, like -ιτις in neur*itis*, periton*itis*, etc., which agrees with νοσος, "disease," understood. In the case of *-itis* an entirely secondary meaning, viz., "inflammation," has been evolved.†

Definition.—Free fluid in the peritoneal cavity.

Incidence.—Ascites occurs in 50 per cent. of all patients dying with cirrhotic livers. Since it is a late event in the course of the disease it naturally occurs far more frequently in cases fatal from the effects of cirrhosis than in patients who, having cirrhotic livers, die from independent disease, such as pneumonia, tuberculosis, erysipelas, etc. Ascites occurs in the vast majority of the cases of cirrhosis which run their full course, but a certain number of cases who die, so to speak, prematurely from the direct effects of cirrhosis, such as hæmatemesis or melæna, do not present ascites.

In Price's‡ 142 cases ascites occurred in 72. In 121 cases of cirrhosis taken from the postmortem records of the Manchester Royal Infirmary, Kelynack § found ascites in 56 per cent. In 166 cases of cirrhosis examined after death at St. George's Hospital ascites was or had been present in 84, or 50.6 per cent. In 80 of these cases death was directly due to the effects of cirrhosis, and in 68 of them, or 85 per cent., ascites was present. In 86 cases where death was due to other factors 16, or 18.6 per cent., had ascites.

Relation between Weight of the Liver and the Incidence of Ascites.—Ascites is much more often found in association with a comparatively small than with large cirrhotic livers. This is due to two factors: (*a*) because in an early stage the liver is often larger than it is later in the disease, and (*b*) because when cirrhosis becomes latent from compensatory hyperplasia of the liver cells the organ is considerably increased in size.

Causes of Ascites.—The factors which give rise to the peritoneal effusion in cirrhosis require some discussion. It will be most convenient to refer to them in order and then briefly to summarize their claims. The factors for consideration are:

(I) Mechanical factors: (*a*) Obstruction to the passage of blood through the liver, due to fibrosis and contraction around the intra-hepatic branches of the portal vein. (*b*) Thrombosis of the radicles of the portal vein in the liver. (*c*) Thrombosis of the trunk of the portal vein.

(II) Toxæmia.

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* McCall Anderson: Contributions to Clinical Medicine, p. 345.

† Compare Buzzard, T.: Trans. Path. Soc., vol. xl, p. 347.

‡ Price, J. A. P.: Guy's Hosp. Reports, Series iii, vol. xxvii.

§ Kelynack, T. N.: Birmingham Medical Review, Feb., 1897.

(III) Concomitant inflammation of the peritoneum and perihepatitis.

(IV) Associated cardiac failure.

(I) (*a*) *Obstruction to the passage of blood through the cirrhotic liver* is an undoubted fact, and leads to chronic venous engorgement of the portal vein area, as shown by the development of a collateral circulation, dilatation, and thickening of the intima of the portal vein, and to some extent clinically by hæmatemesis and melæna. That increased pressure in the portal vein alone does not, however, necessarily produce ascites is shown by experimental ligature of the portal vein in animals.* While in patients with cirrhosis it is noticeable that when the venous pressure in the portal vein appears to be high, as shown by hæmatemesis and melæna, ascites is absent. Further, the extreme rapidity with which the effusion may be poured out—a pint a day in some instances—is hardly compatible with the view that it is solely due to increased venous pressure. If the peritoneal effusion was due to the fibrosis in the liver, it would come on gradually, *pari passu* with the cicatricial contraction of the fibrous tissue around the portal canals, while as a matter of fact ascites often develops suddenly and rapidly.

Since the collateral circulation is a compensatory means of carrying on the circulation, great importance has been attached to it as preventing ascites. But ascites is often present in spite of considerable collateral circulation, and conversely both ascites and evidence of any portal anastomosis may be absent.†

Levi ‡ in a case of cirrhosis with terminal delirium found that there were no ascites and no collateral circulation. It is remarkable that there was peritoneal tuberculosis in addition, which in itself is a sufficient cause of ascites.

For these reasons increased venous pressure due to hepatic obstruction, though very frequently associated with ascites, is not alone a true cause of peritoneal effusion.

(I) (*b*) It has been suggested that the additional factor required to bring about ascites in cirrhosis is thrombosis or obliterating endophlebitis of the terminal branches of the portal vein, either in the liver or where the portal tributaries anastomose with the adjacent systemic veins. There is, however, no proof of this.

(I) (*c*) Thrombosis of the portal vein may give rise to ascites in cirrhosis, but it is so rare that it has no claim to be considered among the important causes of ascites.

In 334 cases of cirrhosis examined after death portal thrombosis was present in 10, or 3.3 per cent. (Langdon Brown.§)

(II) *The Toxic Nature of Ascites.*—As a result of hepatic inadequacy poisons absorbed from the alimentary canal or possibly produced elsewhere are no longer stopped and destroyed by the liver, but pass into the general circulation, and a condition of hepatic toxæmia, analogous to that of renal toxæmia, results; in both these analogous conditions the patients become drowsy and may have numerous hæmorrhages in various parts of the body. In addition, as Hale White* has pointed out, œdema of the feet and sometimes of the abdominal wall occurs. By regarding the poison of hepatic toxæmia as a lymphagogue the occurrence of ascites in cirrhosis may be explained. It is well to lay stress on the fact that œdema of the feet may occur before ascites develops, inasmuch as this shows that the œdema of the feet is not necessarily a mechanical effect due to the pressure of ascitic fluid on the inferior vena cava. The absence of ascites in cases of biliary cirrhosis, where there is some reason to believe that the blood is toxic, viz., the considerable splenic enlargement, is perhaps explained by the fact that the liver cells remain in a better state of nutrition than in portal cirrhosis, and that the poisons, if present, are not necessarily of the same nature as in ordinary cirrhosis.

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* Hale White: Brit. Med. Journ., 1903, vol. i, p. 535.
† Compare Hanot: Archiv. Général. de Méd., 1886, t. clxxvii, p. 603.
‡ Levi: Archiv. Général. de Méd., 1886, t. clxxvii, p. 221.
§ Langdon Brown: St. Bartholomew's Hospital Reports, vol. xxxvii, p. 62.

(III) *Ascites due to Concomitant Inflammation of the Peritoneum.*—In many cases of cirrhosis there is in addition chronic peritonitis, which accounts for the ascites, and especially for ascites which continues for a considerable time or recurs again and again after tapping. Bright, indeed, considered the ascites of cirrhosis to be the result of portal obstruction and of an extension of chronic inflammation from the liver along the portal vein and its branches to the peritoneum. This view in a modified form is held by many authorities, and there is no doubt that ascites is very often satisfactorily explained on this hypothesis. But chronic peritonitis does not account for the onset of ascites in all cases of ordinary cirrhosis, for it is often absent when there is marked ascites. In some cases ascites passes away when the patient is in a semi-comatose condition; now, since chronic peritonitis would give rise to persistent ascites, such cases may be expected to be free from chronic peritoneal inflammation.

The possibility that ascites is due to a low form of secondary infection will require consideration when more is known about the bacteriology of hepatic cirrhosis and of the ascitic effusion which occurs as a terminal phenomenon. This suggestion is attractive from the fact that secondary infections may occur in other parts of the body in the later stages of cirrhosis. From analogy it appears probable that the peritoneum would suffer similarly, since it is decidedly a place of diminished resistance in cirrhosis, and, moreover, infection from the intestinal tract, which is often in a condition of chronic catarrh, might easily occur. Again, ascites may supervene after septic processes have occurred elsewhere in the body, thus suggesting that the ascites is in some way secondary.

Although as seen in laparotomies in cases with ascites the peritoneum is highly injected, there is no inflammation or acute peritonitis. So if there be a microbic origin for ascites, the micro-organisms are not pyogenic, but of a low degree of virulence. It is well to remember that tubercle of the pleura and peritoneum may give rise to almost pure serous effusions, and that in these cases the fluid withdrawn may be almost, if not quite, free from bacilli. Possibly the same may hold for ascites of cirrhosis, viz., that it is due to a micro-organism which does not appear in the fluid withdrawn by paracentesis.

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* Hale White: Clinical Journ., April 26, 1899.

Ascites due to Concomitant Perihepatitis.—Some thickening of the capsule of the liver is commonly seen in cirrhosis, and in some instances satisfactorily explains ascites. But it is not a constant cause; this is shown by the fact that ascites occurs when there is little or no perihepatitis, and that it may be absent when there is as much perihepatitis as there is in cases where the peritoneal effusion is thus explained. Parkes Weber * has suggested that effusion resulting from localized areas of inflammation may possess sufficiently irritating properties to lead to a copious exudation of normal or nearly normal fluid from the non-inflamed surfaces. On this view quite local perihepatitis might account for ascites. Against this view is the fact that foci of perihepatitis often exist in the absence of ascites, both in cirrhosis and in other conditions. Weber has also suggested that transient ascites in cirrhosis may be due to local peritonitis which is temporary and comparable to subacute pleurisy with a serous effusion.

(IV) *Ascites from Cardiac Failure.*—In cases of latent cirrhosis dilatation of the heart from valvular disease, from affections of the myocardium, whether chronic or acute, or from obstructive lung disease may develop and give rise to ascites. The cirrhosis and ascites are therefore associated, but the ascites is not necessarily dependent on the cirrhosis. On the other hand, backward pressure very probably favours the onset of ascites in patients with cirrhosis; in other words, an amount of backward pressure which in an ordinary case would not produce ascites may be the cause of ascites in a patient with progressive cirrhosis. Heart disease may therefore induce ascites in cirrhosis in two ways: (I) Merely by backward pressure, as in some cases of tricuspid regurgitation; (II) by bringing about conditions, such as venous engorgement, the stagnation of toxines, or damage to the endothelial cells of the peritoneum, which precipitate ascites due to cirrhosis.†

In conclusion, ascites may be merely associated with cirrhosis and directly due to chronic or possibly to subacute peritonitis and perihepatitis, or to cardiac failure; in rare cases it may be due to a direct complication of cirrhosis, *i. e.*, thrombosis of the portal vein, or, on the other hand, it may be due to cirrhosis alone. In the latter case it may be explained as being due to a toxic condition of the blood, from the presence in it of poisons having a lymphagogue action, and therefore inducing an exaggerated flow of fluid into the peritoneal cavity. It is probable that this form of ascites may be brought about prematurely by cardiac failure.

The onset of ascites may follow so soon after some event, such as a blow, fall, or exposure to cold, that there would appear to be a definite connexion between them. It is possible that by a blow the resistance of the peritoneum may be so reduced that the real responsible cause of ascites is enabled to produce its effect sooner than it otherwise would. As the result of a chill, vasomotor paralysis of the splanchnic vessels results, and might thus precipitate ascites, so to speak. These cases have been spoken of as acute ascites.[*] It must be remembered that what appears to be acute ascites may prove to be acute peritonitis. Ascites may come on after various infections, such as suppuration, erysipelas, or diseases, such as influenza or typhoid.

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* F. P. Weber: Brain, 1902, p. 150; Edinburgh Med. Journ., April, 1903, p. 322.

† Compare Cheadl, W. B.: Some Cirrhoses of the Liver, p. 103.

Though it may be sudden, the onset of ascites is usually gradual, and is often masked by flatulent distension of the abdomen. It thus contrasts with the sudden and rapid development of ascites in thrombosis of the trunk of the portal vein. Ascites occurs late in the course of uncomplicated cirrhosis, that is, in cases where there is no concomitant chronic peritonitis. The gravity of ascites in such cases has been specially insisted on by Hale White, who finds that the patient seldom survives long enough to require tapping more than once.

Characters of Ascitic Fluid.—The ascitic fluid is clear, greenish or yellow in tint, and sometimes slightly bile-stained. Its reaction is alkaline and its specific gravity between 1008 and 1015. It contains more albumin than ascitic fluid of renal disease and less than that of cardiac ascites (Dickinson[†]). If there is any added peritonitis, its specific gravity and the proportion of albuminous matter increase and flakes of coagulated fibrin may form on standing. It contains from 0.2 to 0.4 per cent. of albuminous material and occasionally a trace of sugar, urea, urobilin. The large amount of chlorides present in ascitic fluid is associated with the diminished amount in the urine. If the specific gravity is above 1015, contains a larger amount of albumin, and microscopically shows polymorphonuclear leucocytes, there is some inflammatory change in the peritoneum.

Character of the Cells in the Ascitic Fluid.—Comparatively little work has been done on the character of the cells found in the ascites of cirrhosis, and the results are not entirely in accord. In one case Dopter and Tanton[‡] found a majority of polymorphonuclear leucocytes and a few endothelial cells. Grenet and Vitry[§] found endothelial cells and a few lymphocytes. Souques,[‖] and Achard and Laubry,[**] in two cases of lactescent ascites in cirrhosis, found lymphocytes and mononuclear leucocytes chiefly represented.

Chylous ascites due to an admixture of chyle is very rare in cirrhosis. When this condition does occur, it is usually associated with malignant disease in the abdominal cavity.

Letulle refers to 3 cases in which cirrhosis was associated with chylous ascites; in Merklem's[††] case of cirrhosis chylous ascites followed a fall, and thus suggests the possibility of laceration of lymphatic vessels, though this was not made out at the autopsy.

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[*] B. Weill: (Acute Ascites) Thèse Paris, 1899, No. 278. Potain: (Ascites a frigore) La Sem. Méd., 1888, p. 9.

[†] Dickinson, W. H.: Allbutt's System of Med., vol. v, p. 668.

[‡] Dopter and Tanton: Bull. Soc. Méd. d. Hôp. Paris, July 12, 1901.

[§] Grenet and Vitry: La Sem. Méd., 1903, p. 235.

[‖] Souques: Bull. Soc. Méd. d. Hôp. Paris, March 21, 1902, p. 290.

[**] Achard and Laubry: Ibid., p. 295.

[††] Merklem: La Sem. Méd., May 12, 1897.

Resembling true chylous ascites in appearance, but differing from it chemically, are the two following forms of ascites: (*a*) the chyliform or fatty, and (*b*) the milky non-fatty ascites; these two forms are not very rare in cirrhosis.

In chyliform or fatty (*adipose*) *ascites* the fat, which is present in larger globules than in the chylous ascites, is probably the outcome of degenerative changes in cells suspended in the ascitic fluid. In cases of fatty ascites in cirrhosis, Souques and Achard and Laubry have found both fat and a nucleo-albumin; the latter gave rise to an opalescent solution. Fatty ascites would thus differ from the next form only in the presence of fat, since it has been thought that in both there is a nucleo-albumin possessing the property of rendering ascitic fluid milky.

In opalescent, milky (*non-fatty*) *ascites*, of which Jousset * has collected fourteen cases in portal cirrhosis, there are a large number of mononuclear leucocytes which probably give rise, as the outcome of degenerative changes, to some body, such as nucleo-albumin or globulin, which is responsible for the lactescent appearance of the fluid. It has, however, been suggested that lecithin may be the cause of the lactescent appearance. (Micheli and Mattirolo.†) No fat can be extracted by ether from the ascitic fluid in this form. In both the fatty and the non-fatty forms of milky ascites the change may appear on the second tapping, in cases where the fluid withdrawn on the first occasion was clear. From the presence of numerous leucocytes in the fluid the exudation has sometimes been spoken of as purulent.

A hæmorrhagic ascites is very rare in cirrhosis. It is not due to mere hepatic insufficiency, like the oozing from the gums and epistaxis. Neither does it appear that it is usually due to concomitant tuberculosis of the peritoneum. It may be the result of previous tapping; thus in cases where the fluid is serous at the first paracentesis and is found to be sanguineous at subsequent tappings, it is probable that the trocar wounded some of the vascular adhesions or dilated veins in the peritoneum forming the collateral circulation. (Barjon and Henry.‡) In some instances of cirrhosis chronic hæmorrhagic peritonitis occurs and possibly may be due to, at any rate is associated with, alcoholism. Fernet § records a case bearing this interpretation.

Bacteriology of Ascitic Fluid.—More observations are required as to the bacteria present in the ascites of cirrhosis, and very probably may be obtained by the new method of inoscopy. It consists in taking the coagulum of the fluid; or, if there is no spontaneous one, producing one, dissolving it with aseptic gastric juice, and examining for micro-organisms; this method depends on the fact that the clot filters off the micro-organisms from the fluid. By this method Jousset ‖ has found tubercle bacilli in many cases thought to be cirrhosis, which is quite in accord with the comparatively frequent incident of tuberculous peritonitis in cirrhosis.

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* Jousset: Quoted by Souques.

† Micheli and Mattirolo: Wiener klin. Wochen., 1900, S. 56. Epitome, Brit. Med. Jour., 1900, vol. i, No. 402.

‡ Barjon et Henry: Lyon Médical, June 10, 1898.

§ Fernet: Bull. de la Soc. Méd. des Hôp., June 22, 1900, p. 781.

‖ Jousset: Archiv de Méd. expériment. et d'anat. path., tome xv, p. 289, 1903.

M. Abbott * found a colon bacillus, of the same type as Adami's minute diplococcus, in the ascitic fluid of three cases of cirrhosis. In one instance, where there was chronic peritonitis as well as hepatic cirrhosis, this micro-organism was isolated from three tappings during life.

Tension of Ascitic Fluid.—There may be a positive pressure inside the abdomen in ascites, as shown by the upward displacement of the diaphragm.

Pitres † has measured this manometrically, and finds that it may vary between 30 and 6 millimetres of mercury, the average positive pressure being about 12 millimetres.

This positive intra-abdominal pressure, of course, varies with respiration and is associated with increased tension in the portal vein and low arterial pressure. (Gilbert et Weill.‡)

Physical Signs.—The abdomen is greatly enlarged; its girth may be fifty inches or even more. The enlargement is uniform, but is perhaps more marked antero-posteriorly than laterally. The parietes are stretched and the skin often shows the effects of distension in lineæ albicantes, which become especially visible after paracentesis. The abdominal muscles become lax and atrophied and the umbilicus may become everted and project like a tense thin-walled bladder; it may become ulcerated, and has been known to burst. The veins over the umbilicus are sometimes very prominent. The loss of tone in the abdominal parietes allows flatulent distension to occur, especially after the intra-abdominal pressure has been reduced by paracentesis. The costal margins are pushed forwards and the ensiform cartilage may be carried upwards and forwards. The subcutaneous veins of the abdominal walls become prominent and enlarged. There are two sets of veins: (*a*) Those around the umbilicus. This is part of the compensatory anastomosis between the veins of the abdominal wall and the parumbilical veins in the falciform ligament. To a dilated and varicose condition of the veins around the umbilicus the term cirsomphalos has been applied. (*b*) The veins running up from the middle of the groin (the superficial and deep epigastric veins) towards the middle of the costal arch (superior epigastric and long thoracic veins). The dilatation of these veins points to obstruction to the passage of blood through the inferior vena cava. A large ascitic effusion may, by increasing the intra-abdominal pressure, seriously interfere with the return of blood from the lower extremities, and so lead to opening up of this anastomotic channel.

The ascitic fluid presses the diaphragm up and diminishes the capacity of the thorax. The heart may thus be displaced upwards so that its apex-beat is in the third interspace. This displacement may be associated with a systolic murmur over the pulmonary artery, due to twisting or kinking of its trunk. When the displacement is corrected by tapping, this murmur disappears.

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* Abbott, Maude: Journal of Path. and Bacteriol., vol. vi, p. 315.
† Pitres: Soc. de biolog., July 22, 1899, p. 674.
‡ Gilbert et Weill: Soc. de biolog., June, 1899, p. 511.

The liver dulness is displaced upwards into the thorax and anteriorly may reach to the fourth, third, or even second rib, while posteriorly the resonance over the bases of both lungs is also encroached upon. If there is dulness over the lower lobe of the right lung alone, the question arises whether this is due solely to upward displacement of the liver and collapse of the lung or whether there is not, as is often the case (*vide* p. 282), an effusion into the right pleural cavity. If the patient be directed to take a deep breath, the dulness will remain unaltered if there is an effusion, but will diminish somewhat if due solely to the liver; in addition, in pleural effusion the dulness is higher in the axilla, while the dulness due to the liver is more marked behind.

In women, the uterus is pressed forwards by the fluid in Douglas' pouch, and depressed, and may thus become prolapsed.

The fluid collects in the flanks and gives rise to a dull note on percussion. In order to distinguish ascites from fæcal distension of the colon the patient should be turned over, when the note will become resonant; this shifting dulness is proof of free fluid in the peritoneal cavity. It should be pointed out that in a certain proportion of cases of ascites there is resonance in one or both flanks, due to gaseous distension of the colon. The absence of dulness in the flanks, therefore, must not be taken as absolute evidence against ascites and in favour of an ovarian cyst.

After collecting in the flanks the fluid rises out of the pelvis and gives rise to a dull note on percussion. This dull area gradually increases in extent and approaches the umbilicus. The stomach and intestines are floated upwards against the abdominal parietes in the middle line between the umbilicus and the ensiform cartilage. The area of resonance eventually roughly corresponds with that of the epigastric region. Chronic peritonitis may be combined with cirrhosis, and if well marked may lead to such retraction of the mesentery that the intestines, being more or less tethered to the spine, are unable to reach the anterior abdominal wall; in such cases there may be complete absence of resonance over the front of the abdomen.

When there is more than a small quantity of ascitic fluid in the abdomen a thrill is readily produced by flipping the abdominal wall in one flank with the finger; a distinct impulse is then felt by the other hand laid flat on the skin of the opposite side. In order to prevent the impulse from being transmitted merely through the abdominal walls, an assistant should place his hand or a piece of cardboard on the linea alba in the long axis of the body. When the abdominal wall is laden with fat or swollen from subcutaneous œdema, the precaution is especially necessary. When old peritoneal adhesions are present, the ascitic effusion will very probably become encysted. The physical signs may then resemble those of a fixed cyst, and are very difficult to interpret correctly. Encysted ascites is, however, rarely seen in connexion with hepatic cirrhosis.

When there is free fluid in the peritoneal cavity, it is found under certain conditions that if the hand is placed flat over the liver and a sudden sharp flexion of the fingers made, a sensation of displacement of fluid is produced and the finger-tips come in contact with the firm liver. This sign—"dipping for the liver"—often cannot be obtained. It depends on the presence of fluid between the liver and the abdominal wall. Hence adhesions between the liver and the parietes, or the fact that the liver is in immediate contact with the abdominal wall, prevents this manifestation of ascites.

Symptoms and Effects of Ascites.—There is a feeling of tightness and discomfort in the tense and stretched abdominal walls, which, like other bad effects of ascites, are due to the pressure exerted by the fluid. The upward displacement of the diaphragm gives rise to collapse of the lower lobes of the lungs, and so to dyspnœa, and even to orthopnœa of slight degree. There is often some bronchitis, and in rare instances hæmoptysis may result from the engorged and collapsed lung. In cases where, with increasing ascites, signs of œdema of the lower parts of the lungs—râles—develop, the abdomen should be tapped without delay.

The upward displacement of the heart may be accompanied by irregularity, palpitation, or faintness. The pressure of ascites on the kidneys and their vessels may help to diminish the excretion of urine and possibly to produce albuminuria, but the diminished amount of urine is chiefly due to the low arterial pressure. Œdema of the legs may be accelerated by the pressure of the peritoneal effusion on the inferior vena cava, but it is not solely due to this mechanical cause, inasmuch as œdema of the feet may precede the appearance of ascites, or indeed occur independently. As is pointed out elsewhere, toxæmia plays an important part in the production of œdema of the feet.

If ascites is allowed to become very excessive, the umbilicus, which has become everted and thin, may burst; this spontaneous discharge has also been known to take place through the cicatrix of an umbilical hernia. (Merklem and Gougelet.*) Such an event should never be allowed to occur; not only is the extreme distension very harmful, but the rupture of the abdominal wall is very likely to be the means of introducing infection, and so setting up fatal peritonitis. Most of the recorded cases occurred years ago, when paracentesis was postponed as long as possible.

Differentiation of Ascites from Other Abdominal Conditions.—There are a very fair number of conditions that have at one time or another simulated ascites. The most likely to imitate ascites are ovarian cysts, large peritoneal lipomata, and encysted peritonitis, of which the first is the only frequent cause of error.

1. A large, thin-walled *ovarian or parovarian cyst*, if so large as to nearly fill a great part of the abdomen, may give rise to great difficulties in diagnosis. In the case of an ovarian cyst the history may show that the swelling was definitely noticed to begin in one situation, that it arose out of the pelvis and then spread upwards. The outline of the cyst may be felt or may be made out on deep inspiration. In a doubtful case a vaginal examination may reveal a cyst with pelvic attachments.

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* Merklem and Gougelet: Bull. Soc. Méd. des Hôp., July 19, 1901, p. 952.

The abdomen is prominent in an anteroposterior direction, while in simple ascites the bulging is also in a lateral direction.

The dulness is in or near the middle line of the abdomen and not in the flanks; but, as already pointed out, resonance in the loin may persist in ascites. The maximum abdominal girth is below the umbilicus, while in ascites it is at or above this level. In ascites the umbilicus is in its normal position, viz., one inch nearer to the pubes than to the ensiform cartilage, while with an ovarian cyst this relation may be greatly altered in the opposite direction. When an ovarian cyst is situated on either side of the middle line, it may displace the umbilicus, so that it is nearer one anterior superior spine than the other. This displacement may only be revealed by careful measurement, and not be manifest on mere inspection.

In ovarian cysts the thrill may be absent, and when present is less marked than in ascites. There is little constitutional disturbance in ovarian cysts, the ill effects being almost entirely due to mechanical pressure. When an ovarian cyst, as is sometimes the case, is complicated by ascites, the diagnosis is extremely difficult. Rupture of the cyst with extravasation of its contents into the peritoneal cavity may occur spontaneously in thin-walled cystadenomata and parovarian cysts, or from traumatism. If the fluid is non-irritating, it is absorbed, with the result that polyuria follows; but if irritating, peritonitis is set up. A rare event is fatal intraperitoneal hæmorrhage.[*]

2. *Solid or Semisolid Abdominal Tumors Simulating Ascites.*—Fatty, fibro-fatty, and myxolipomatous tumors, though comparatively rare, may, when they grow to a considerable size,—and some of them have weighed as much as 40 pounds,—very closely imitate ascites. In fact, many of the recorded examples have been tapped fruitlessly, and several of them more than once. Of the fatty tumors, of which Adami[†] has collected 42 examples, about one-third arise from the fat around the kidneys; the remainder take origin from the retroperitoneal and other tissues. The tumors, whether originally fatty or fibrous, are prone to become œdematous and undergo myxomatous degeneration and so readily fluctuate.

Diffuse colloid carcinoma of the peritoneum is very rare; it may give rise to great enlargement of the abdomen and to dulness on percussion, but fluctuation and thrill are not present unless there is concomitant ascites. In some cases there is no difficulty in feeling definite tumors, and then there is no resemblance to ascites.

Pye Smith[‡] refers to a case of colloid carcinoma involving the peritoneum where tapping was performed thirty-six times. Sometimes colloid material blocked the cannula.

Encysted peritonitis and the localized tuberculous peritonitis in the lower and front portions of the abdomen[§] (Tait's allantoic cysts) differ in the extent of the peritoneal cavity involved and in the fact that the dulness due to the effused fluid does not alter with changes in the position of the patient.

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[*] Kelly, H. A.: Operative Gynæcology, vol. ii, p. 253.

[†] Adami: Montreal Medical Journal, Jan., Feb., 1897

[‡] Pye Smith: Trans. Path. Soc., vol. xliv, p. 117.

[§] Doran A.: Medico-chirurg. Trans., vol. lxxxi, p. 320.

Hydatid Cysts.—Murchison describes an enormous cyst starting from the liver and passing through the foramen of Winslow into the general peritoneal cavity, which it almost filled. In its fully developed or latest stage it resembled ascites, but the history showed that the abdominal swelling was at first localized to the right side.

Various abdominal cysts, such as pancreatic, omental, chylous, urachal, mesenteric cysts, are comparatively seldom so large as to resemble ascites. A large pyonephrosis or hydronephrosis is so unilateral that it should not be mistaken for ascites. In very exceptional instances a dilated stomach, a dilated gall-bladder, and a very large hepatic abscess have been diagnosed as ascites. Cases of large hepatic abscesses which were at first thought to be ascites have been recorded by Powell * and Hatch.†

From a Pregnant Uterus with Hydrops Amnii.—The outline of the enlarged uterus may be made out by palpation through the abdominal walls. Other signs of pregnancy, such as mammary enlargement and engorgement, soft and patulous os uteri, enlarged uterus, should be looked for.

Obesity.—When the abdominal walls are laden with fat, the detection of a small amount of ascitic fluid is difficult and often impossible. On the other hand, a feeling of semifluctuation may be obtained through the pendulous fatty walls and suggest ascites. To control this the hand of an assistant should be placed with the ulnar side downwards on the abdominal wall between the two hands of the observer so as to prevent any fluctuation from being conducted through the parietes. Inspection alone should assist in the diagnosis. When there is much fat in the abdominal parietes, the umbilicus is buried, while in ascites the umbilicus tends to be everted.

Diagnosis of Ascites Due to Cirrhosis from that Due to Other Causes.—Under the following heads attention will chiefly be paid to the main points that are in favour of the various conditions which may imitate cirrhosis by inducing ascites.

Acute peritonitis can hardly be confounded with the ascites due to cirrhosis, for the onset is sudden, the constitutional symptoms are prominent, and the abdominal distension is due to paralytic dilatation of the intestines with gas rather than to the quantity of fluid. It should be mentioned, however, that ascites may sometimes come on rapidly in the course of cirrhosis, especially when complicated by portal thrombosis. Unlikely as it would appear, sudden ascites developing in a case of alcoholic cirrhosis in which there was subacute gastritis has simulated intestinal obstruction. (*Vide* p. 288.)

The ascites due to the various forms of *chronic peritonitis* is extremely likely to be mistaken for that of cirrhosis. Chronic peritonitis and universal perihepatitis (*vide* p. 164) frequently cause ascites, usually in association either with adherent pericardium or with arteriosclerosis and granular kidney. The physical signs of these conditions should therefore be looked for. In a doubtful case albuminuria is therefore against the existence of cirrhosis as a primary cause. In chronic peritonitis the ascites recurs again and again after tapping; cases are on record where the abdomen has been tapped fifty or even a hundred times. This is the most reliable criterion in distinguishing chronic peritonitis from cirrhosis. Enlargement of the spleen, which is comparatively frequent in cirrhosis, is not a prominent feature in chronic peritonitis, unless there is some complication, such as lardaceous disease. Hæmatemesis hardly ever occurs in chronic peritonitis; hence the association of hæmatemesis and ascites points to cirrhosis. In cases where hæmatemesis is associated with frequently recurring ascites chronic peritonitis is probably complicated by some other condition, such as gastric ulcer or cirrhosis.

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* Indian Med. Gaz., Feb., 1898.

† Ibid., Aug., 1898.

Tuberculous peritonitis may supervene as a secondary infection in the course of cirrhosis, and is then very likely to be regarded as simple ascites. Thus in 121 cases of common cirrhosis in adults Kelynack found that active peritoneal tuberculosis was in progress in 12. The primary lesion here is cirrhosis, which disposes the peritoneum to tuberculous infection. In these cases the liver is markedly cirrhosed, while the peritonitis is of more recent date. In cases of tuberculous peritonitis a slight secondary hepatic fibrosis is sometimes seen, but is microscopic rather than macroscopic. Tuberculous peritonitis alone is commoner in children than in adults, while cirrhosis is rare in children.

The mistake that has often occurred is to do laparotomy on a child with cirrhosis and ascites in the belief that it is tuberculous peritonitis. If such a thing occurs, it would be advisable to take the opportunity of uniting the liver and great omentum to the abdominal wall so as to lead to vascular adhesions. (*Vide* p. 257.)

Tuberculous peritonitis in adults, except when secondary to cirrhosis, is most often seen in women, and often spreads from the uterine appendages. Search should be made for evidence of tuberculosis elsewhere. The following points are in favour of tuberculous peritonitis: abdominal pain and tenderness, especially in the lower part of the abdomen and about the right iliac fossa; pain on micturition; fever; palpable, enlarged glands in the abdomen or groin, and a moderate degree of effusion; a hard cord due to the rolled-up transverse colon; induration around the umbilicus, redness of the skin, and evidence of a small abscess in this situation. When drawn off, the fluid is more turbid and is often seropurulent, of a higher specific gravity (1020 instead of 1010), and richer in albumin than in cirrhosis. Ordinary examination for tubercle bacilli is often negative, but injection into guinea-pigs gives rise to tuberculosis. It is probable that the method of inoscopy,* or bacterial examination of the clot formed in the fluid, will give positive results in cases where ordinary methods fail.

In ascites due to multiple nodules of malignant disease in the peritoneum a primary source should be manifest in the stomach (symptoms of dyspepsia, pyloric obstruction, absence of HCl in vomit), in the rectum, and in women in the uterine organs. The umbilicus may be hard and infiltrated with growth, and sometimes small subcutaneous tumors can be felt in the line of the falciform ligament or elsewhere in the abdomen. It must be remembered that small masses of fat may very closely imitate these minute secondary growths. In malignant disease there is more emaciation and more frequently pigmentation of the face than in cirrhosis. In some instances of malignant disease in the abdomen there is the peculiar warty and pigmented condition of the skin known as "acanthosis nigricans." The spleen is not enlarged and there is no history of hæmatemesis. Sometimes glands in the groin may be enlarged, and occasionally multiple subcutaneous tumors are present.

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* Jousset: Archiv de Méd. expériment. et d'anat. path., tome xv, p. 289.

In *malignant disease* of the liver the presence of deep jaundice together with ascites, the enlargement and irregularity of the liver, the progressive hepatic enlargement and more rapid emaciation, help to differentiate it from ascites due to cirrhosis. Other points in favour of malignant disease are evidence of growth elsewhere, induration of the umbilicus, and absence of splenic enlargement. In cases which come under observation at a late stage with ascites it is often impossible to determine whether there is cirrhosis or malignant disease of the liver until the abdomen has been tapped. A large nodular liver points to new-growth.

Syphilitic disease of the liver may give rise to ascites. The presence of syphilitic lesions elsewhere should always be the signal for a course of antisyphilitic treatment, which may clear up the diagnosis. When enlarged from gummatous or lardaceous change, or from both combined, the liver is firm and may be irregular, and is not unlikely to be mistaken for malignant disease.

Lardaceous disease of the liver does not often give rise to ascites. The following case of lardaceous liver closely imitated cirrhosis:

A woman aged forty-seven under my care in St. George's Hospital, June–July, 1900, had the facial aspect of cirrhosis; there were signs of chronic pulmonary tuberculosis at both apices, œdema of the feet which preceded by two weeks the onset of ascites, and albuminuria. There was a history of hæmatemesis which in the light of the autopsy was probably hæmoptysis. There was extreme ascites which required tapping twice; the liver and spleen could not be felt. The patient was thought to have cirrhosis. Death took place from asthenia, the patient being semicomatose. The autopsy showed lardaceous disease of the liver (53 ounces) and kidneys, which was accounted for by chronic pulmonary tuberculosis, with 3 or 4 vomicæ in both upper lobes. There were slight thickening of the capsule of the liver and opacity of the peritoneum, but not enough chronic peritonitis to account for the ascites. There was no cirrhosis of the liver.

The history of past suppuration or of syphilis, evidence pointing to lardaceous disease of the kidneys (albuminuria) or of the intestines (diarrhœa), are important points in making a diagnosis.

Thrombosis of the Portal Vein.—This is a rare condition, but when it does occur is associated with portal cirrhosis of the liver in about 37 per cent. of the cases. When the trunk of the portal vein is affected, ascites, if not already present, rapidly develops. The spleen enlarges from obstruction of the splenic vein and hæmatemesis may occur. The severity of the symptoms and their onset in a person whose past history shows neither cause for nor evidence of cirrhosis would be in favour of primary thrombosis of the portal vein. But it will always be difficult to be sure that the case is not one in which cirrhosis has remained latent.

The difficulty or impossibility of a correct diagnosis in some cases of portal thrombosis supervening in the course of cirrhosis is illustrated in the following case:

A man aged fifty-six in a state of great weakness and considerable emaciation was admitted under me at St. George's Hospital on January 28, 1902, complaining of "dropsy, stoppage of the bowels, and difficulty in passing water." He had noticed œdema of the feet five weeks before; this was followed by constipation and difficulty in passing water. He had been quite a moderate consumer of beer, and denied syphilis. He was found to have marked ascites; nothing abnormal could be felt in the abdomen and he was thought to be probably the subject of malignant abdominal disease. Almost directly after admission he began to wander in his mind, and shortly afterwards became moribund, dying about thirty-six hours after admission. At the autopsy there were chronic peritonitis, marked portal cirrhosis, and thrombosis of the portal vein; the liver weighed 4 pounds and the spleen 4 ounces.

Ascites from ovarian papillomata may recur very frequently, and is thus different from the ascites of uncomplicated cirrhosis. The diagnosis can be clinched by vaginal or rectal examination and the detection of irregular masses of growth choking up the pelvis, or by the recognition of pieces of the characteristic villous growth in fluid withdrawn from the abdomen.

Dr. Pye Smith * has recorded a remarkable case of papillomatous tumors of both ovaries which gave rise to ascites in a woman aged thirty-five lasting nine years and necessitating 299 tappings. At the autopsy there were numerous implantation growths over the parietal peritoneum.

Ascites due to backward pressure of tricuspid regurgitation, etc., should be recognised by examination of the heart and the recognition of mitral or obstructive lung disease—emphysema, chronic interstitial pneumonia, or pneumonokoniosis. In some cases of cirrhosis failure of the heart, such as may occur from alcoholism, may induce ascites, so that cirrhosis and ascites are associated, though not necessarily related, as cause and effect. In such cases it is difficult to decide their relationship until the alcoholic dilatation of the heart has been successfully treated.

In *renal disease* ascites is part of the general dropsy which typically affects the face. The character of the urine and the cardiovascular changes proper to renal disease should prevent any mistake in diagnosis. As pointed out elsewhere (Associated Lesions, p. 223), renal disease may coincide with portal cirrhosis.

In *splenic anæmia* of adults, which is a distinctly rare disease, ascites very occasionally appears before the terminal cirrhosis of the liver, which is known as Banti's disease, has developed, as shown by postmortem examination of cases of uncomplicated splenic anæmia. Inasmuch as periodic hæmatemesis also occurs in that disease, the resemblance to cirrhosis when ascites develops might be thought to be very close. Clinically the anæmia and splenic enlargement are so much greater in splenic anæmia that ordinary cirrhosis is only likely to be diagnosed by those who are not familiar with the fact that ascites and periodic attacks of hæmatemesis may occur in splenic anæmia.

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* Pye Smith: Trans. Path. Soc., vol. xliv, p. 111.

Prognosis of Ascites.—The prognosis of ascites due to cirrhosis is very bad; as a rule, death follows within a short time of its onset—usually within two months, and sometimes much sooner.

A distinction has rightly been drawn, more especially by Hale White * and Campbell Thomson,† between ascites due to cirrhosis in which the prognosis is of the gloomiest character, and ascites associated with cirrhosis, but due to some other cause, such as chronic peritonitis. In ascites associated with chronic peritonitis tapping may be required frequently, and occasionally recovery may occur, while in ascites due to cirrhosis tapping is seldom required more than once, and is soon followed by death.

Since œdema of the feet in the course of cirrhosis is a sign of general toxæmia, the prognosis in a case of cirrhosis with ascites and œdema of the feet is much worse than in cirrhosis with ascites alone, inasmuch as the latter may be a case of cirrhosis associated with ascites due to some other factor, such as chronic peritonitis. The presence or absence of œdema of the feet may thus be useful in determining whether, in any case of ascites due to cirrhosis, the case is likely to terminate rapidly, or whether several tappings may be required with a possible, though frail, chance of recovery.

In the section on the general prognosis in portal cirrhosis the prognosis of ascites is referred to again.

The Treatment of Ascites.—The treatment of ascites may be divided into:

(I) By paracentesis.

(II) By the operation for producing vascular adhesions around the liver.

(III) By diuretics and purgatives.

The first and last of these methods are merely directed to the removal of the ascitic fluid. The production of artificial vascular adhesions is intended to prevent the peritoneal exudation, and is therefore a more radical method.

Advisability of Performing Paracentesis.—Formerly paracentesis of the abdomen was postponed as long as possible, partly because infection of the peritoneum sometimes followed tapping, and partly because the patient often went down-hill extremely rapidly after the withdrawal of the ascitic effusion. With antiseptic precautions the likelihood of peritonitis resulting is minimised, while the occurrence of death comparatively shortly after paracentesis must be considered to be due to the natural course of the disease, and not to the removal of ascites.

Other reasons given for only adopting paracentesis as a last resource were that (*a*) the removal of fluid entailed the loss of a considerable amount of albumin, an argument that might also be used against opening an abscess (Murchison), and (*b*) that the intra-abdominal pressure of ascites prevented further transudation of fluid (Frerichs). Opinion has changed, and at the present time tapping is performed as soon as it is required in order to prevent the bad effects of excessive ascites.* It is a much more effective method than purgation or the attempt to drain off the fluid by the kidneys and does not tend to weaken the patient's strength as violent purging does.

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* Hale White: Guy's Hosp. Reports, vol. xlix, 1892.

† Thomson, Campbell: Medico-Chirurg. Trans., vol. lxxxiv, p. 251.

Bad Effects of Excessive Ascites.—The results of ascites have been already referred to; they are largely mechanical in the first instance and due to pressure on the abdominal and thoracic viscera; the functions of these organs are interfered with and are therefore imperfectly performed. The renal veins are pressed upon and the urinary excretion impeded, much in the same way as in the backward pressure of heart disease. It is probable that this mechanical venous engorgement of the kidneys, due to the pressure exerted by the ascitic effusion on the renal veins, accounts for the fact that diuretics often fail to remove ascites at first, though they may be more successful in producing diuresis when given after paracentesis has been performed.

Indications for Paracentesis.—When the patient complains of marked discomfort, the abdomen should be tapped, but apart from this there are other conditions, such as diminished amount of urine associated with œdema of the legs, signs of thoracic embarrassment, such as dulness at the bases of the lungs due to collapse, dyspnœa, râles at the bases of the lungs, and in rare instances hæmoptysis from collapse of the lungs, which should make the practitioner tap the abdomen. In cases where with abundant ascites, hæmatemesis occurs, the abdomen should be tapped, as by this means venous engorgement may be diminished.

Method of Performing Paracentesis.—The most satisfactory treatment is tapping the abdomen with a Southey's trocar and cannula and allowing the fluid to drain slowly away through a fine india-rubber tube into a bucket which is placed by or underneath the bed. It occasionally happens—I have seen three such cases—that the abdominal wall is so enormously thick that a Southey's trocar fails to reach the peritoneal cavity, and that a specially long trocar is required. In one such case where I used the trocar of a Dieulafoy's aspirator the abdominal wall, as it became lax from the removal of the ascitic fluid, collapsed in thick folds on the trocar and bent it out of shape.

The skin should be carefully washed and an antiseptic dressing (1 in 40 carbolic) put over the area where the trocar is to be introduced, and the trocar and cannula should be boiled in a test-tube containing water and left to cool in a solution of carbolic 1 in 40. The trocar is usually inserted in the middle line between the symphysis pubis and the umbilicus, but sometimes, from the presence of omental or other adhesions, little or no fluid may be drawn off in this situation; in such instances it will be necessary to tap the abdomen in the linea semilunaris on one or other side. It has been suggested that the spot selected should be on a line joining the umbilicus and the anterior superior spine of the ilium on the left side, so as to avoid any danger of wounding the cæcum or the liver (Plicque*). It is, of course, essential that the area selected should be dull, and it should be ascertained, if necessary by passing a catheter, that the dulness is not due to a distended bladder.

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* Austin Flint was the first vigourous advocate of tapping comparatively early in the course of the disease. *Vide* American Jour. Med. Sciences, 1863, and Brit. Med. Jour., 1883, vol. ii, p. 565.

Under ordinary conditions and with reasonable care there should never be any danger of wounding the liver. I have, however, seen its effects at a postmortem in which there was very considerable extravasation from puncture of a large branch of the portal vein. As a rule, little or no harm results.

Goodhart,† indeed, refers to the case of a woman who when apparently in a very advanced stage of the disease was tapped, but only blood came away, and it was thought that the trocar had passed into the liver. However, from that time the patient steadily improved. Possibly this fortunate result was due to the wound producing vascular adhesions around the liver.

The patient lies on his back and the cannula should be fixed by means of plaster. During the drainage the abdomen should be compressed by a many-tailed bandage, or by a binder which must be tightened from time to time, so as to avoid tympanites.‡ When the cannula has ceased to run from the small amount of fluid left in the abdomen, and not from displacement or blocking of the tube, which can be ascertained by passing a probe down the cannula, it should be withdrawn and the small wound covered with a plug of absorbent cotton-wool saturated with collodion. The binder should be kept on for two or three days to prevent flatulent distension of the intestines. If any distension occurs, a dose or two of the sulphates of magnesium and sodium, a drachm and a half of each, should be given. If the abdomen is nearly emptied, the small trocar wound heals up, and no trouble from leakage results. When, however, from adhesions the fluid is not satisfactorily removed, I have seen considerable inconvenience from leakage from the wound, although the cannula had ceased to run. After paracentesis, from the increased absorption of fluid from the bowel and from the flaccid condition of the abdominal muscles, there is occasionally troublesome constipation.

Use of a Large Trocar.—In former times a large trocar, like that employed for withdrawing the contents of an ovarian cyst, used to be plunged into the abdomen and the fluid rapidly drawn off. This is chiefly of historical interest; personally I have never seen it employed. The rapid withdrawal of fluid sometimes led to collapse, possibly from a large quantity of blood being drawn into the splanchnic veins.

Treatment by Continuous Drainage.—The wound has been kept open and the fluid allowed to run away continuously by Caillié of New York,

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* Plicque: La Presse Médicale, Jan. 13, 1900, p. 28.

† Goodhart: Guy's Hospital Gaz., June 7, 1897.

‡ This practice appears to have been first employed by Dr. R. Mead. See "The Gold-headed Cane," 2d ed., p. 73, 1828.

Elliot of Boston, Urso, Cheadle,* and others. This has also been recommended in the operative treatment of ascites due to cirrhosis by producing vascular adhesions, so as to prevent disturbance of the adhesions. But it has grave drawbacks.

In 9 cases of Urso's, 4 died directly; the best result seems to have been prolongation of life for nine months. Elliot's cases were both fatal. Cheadle says that in some of his cases where the puncture of paracentesis has remained open the results have been satisfactory except for the manifest discomfort involved.

A modification of permanent drainage is described by Jaboulay † under the title "Cicatrice à filtration." A man with ascites from cirrhosis was operated upon in the following manner: The skin of the abdomen was incised transversely below the left costal arch, the muscles and peritoneum were divided lower down, and a piece of omentum was attached outside the peritoneal cavity, and the wound closed with hardly any escape of ascitic fluid. The skin healed over the artificially produced interstitial hernia of the great omentum and the ascites diminished by escaping into the subcutaneous tissues of the abdominal wall. About a week after the operation a small external fistula in the stitch wounds developed and the fluid gained an external exit. The man left the hospital in fair health.

The Surgical Treatment of Ascites by the Production of Vascular Peritoneal Adhesions.—This method of treatment, as conceived by Drummond and Morison,‡ was based on the assumption that ascites was due to portal obstruction, and was an attempt to increase the collateral circulation between the radicles of the portal vein and the general systemic veins. The operation was original in Morison's hands, but it appears that it had been previously planned by Talma and carried out by Van der Meulen in 1889, by Schelkley in 1891, and by Lens in 1892. It is often spoken of as Talma's operation, or as the Talma-Morison operation, but there is no doubt that Drummond and Morison first brought it into notice in England and America.

Technique of the Operation.—It is convenient to tap the abdomen before the operation is performed so as to remove the ascites, though this is by no means essential. An incision parallel to the right costal margin is probably more convenient than one in the long axis of the body. The liver should be examined so as to confirm the diagnosis of cirrhosis, for the operation will do no good if the cause of the ascites is chronic peritonitis. The peritoneum over the liver and diaphragm is scraped or curetted so as to set up adhesive inflammation, and the surfaces are brought in contact by stitching the round ligament to the abdominal parietes or by passing stitches through the liver itself. It appears that it is a distinct advantage to utilise the great omentum as a means of multiplying the vascular adhesions; in order to accomplish this, the omentum is interpolated between the diaphragm and the convexity of the liver. There are numerous veins in the great omentum which will assist in the development of a compensatory anastomosis. No bad effects, such as intestinal obstruction, result from limitation of the scope of the transverse colon's movement. This was, I believe, first carried out in a case operated upon by my colleague, Mr. G. R. Turner.* In a case operated upon by Talma† the spleen remained of considerable size until he did a second laparotomy and sutured the spleen to the abdominal parietes, after which it became smaller. It has therefore been thought that the peritoneum should be scraped widely so as to allow of vascular adhesions forming around the spleen as well as around the liver. The peritoneal cavity should be drained either by means of a glass tube inserted into the wound or by a separate suprapubic incision into the peritoneum so as to prevent the ascitic fluid separating the roughened peritoneal surfaces and interfering with the formation of vascular adhesions. The patient should also, as far as possible, be kept in a sitting posture, so as to prevent re-accumulation of fluid in the upper part of the abdomen.

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* Cheadle: St. Mary's Hosp. Gaz., May, 1896. Brit. Med. Journ., 1900, vol. i, p. 895.

† Jaboulay: Lyon Médical, tome xciv, p. 499.

‡ Drummond and Morison: Brit. Med. Journ., 1896, vol. ii, p. 728.

It has been suggested by Murrell ‡ that the development of a collateral circulation may be accelerated by rubbing the skin of the abdomen with ung. capsici or with cajeput oil. This would, of course, not be done until the operation wound had completely healed.

Epiplopexy is the name applied by J. B. Roberts § to a slighter operation which requires less manipulation and is therefore applicable to advanced cases with little power of resistance. Its object is to increase the compensatory collateral circulation between the radicles of the portal veins and the systemic veins. The operation consists in suturing the great omentum to the anterior abdominal wall. Roberts performed this operation in two cases, in one with very temporary relief, in the other death occurred within forty-eight hours of the operation.

Discussion of the Manner in which the Operation Improves the Condition of the Patients.—Does the improvement which sometimes results both in the general health and in the local condition—viz., the disappearance of ascites—simply depend on the collateral circulation relieving the pressure in the portal vein? This was the assumption on which Drummond and Morison planned their operation, and more recently it has been emphasised by Weir. ‖ Against this it may be argued (*a*) that ascites does not occur when the blood-pressure is presumably highest in the portal vein—viz., earlier in the course of the disease when hæmatemesis is most often met with, and that experimental ligature of the portal vein does not necessarily produce ascites. Cirrhosis may exist for many years without ascites, which may appear quite suddenly; while if ascites was a purely mechanical effect of increased venous pressure in the portal vein, it should develop gradually and earlier in the course of the disease. It therefore would appear that the good effects of the collateral circulation are not solely due to relieving the pressure in the portal vein. (*b*) That ascites is a late manifestation and appears to be rather a result of a toxæmic condition of the blood than a mere mechanical result of increased portal blood-pressure, and that it is the outcome of a poison in the plood exerting a lymphagogue action.[*] The toxæmic state depends on hepatic insufficiency—in other words, on the cirrhotic liver being unable to destroy poisons that are continually passing to it from the alimentary canal; these poisons, therefore, reach the general circulation and lead to œdema of the feet, ascites, and to the constitutional and nervous symptoms of the late stages of cirrhosis. If the collateral circulation between the peripheral parts of the portal vein and general systemic veins is markedly increased, less blood will go through the liver and the toxæmia will be increased. In fact, the collateral circulation between the portal and general venous system is carried to its logical conclusion in Eck's fistula. In this experiment the portal vein is interrupted in the portal fissure; its proximal end is closed, while its distal end is put into communication with the inferior vena cava. In other words, the portal circulation through the liver is short-circuited and all the blood from the intestinal area enters directly into the inferior vena cava. As shown by the very successful experiments of Hahn, Nasse, Nencki, and Pawlow[†] on dogs, this procedure tends to induce a disposition to uræmia. Thus if the dogs were fed on meat, severe nervous disturbance, depression, asthenia, clonic and tonic spasms, and coma were brought on and sometimes, indeed, ended in death. It is noticeable that one of Morison's[‡] patients was alternately excited and depressed for three weeks after the operation; similar depression has been noted in other cases, and may be explained as being due to the passage of poisons, manufactured in the intestine, directly into the general circulation without the intervention of the liver.

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* Rolleston and Turner: Lancet, 1899, vol. ii, p. 1660.
† Talma: Berlin. klin. Wochen., Sept. 19, 1898, S. 833.
‡ Murrell: Lancet, 1902, vol. i, p. 1602.
§ Roberts, J. B.: Philadelphia Med. Journal, Jan. 26, 1901, p. 163.
‖ Weir: Medical Record, 1899, p. 149.

Thus, since it appears that the increase in the collateral circulation between the portal vein and the general systemic system would tend to induce a general toxæmia, the improvement in general health that follows the operation must be due to some other cause than the formation of anastomotic channels between the portal vein and the general systemic veins.

Thomson[§] has suggested that the operation may prevent ascites by the simple methcd of producing universal adhesions and obliterating the peritoneal cavity. That this is a possible method is shown by the cases, such as Dickinson's[‖] and Weber's,[**] in which ascites disappeared and cirrhosis with universal peritoneal adhesions was found at the autopsy.

In a paper written in 1899 by Mr. G. R. Turner and myself it seemed probable that there were two other ways in which the development of a collateral circulation in adhesions around the liver might be beneficial to the economy: (1) By somewhat diminishing the flow of blood through the liver it may enable that organ to deal more satisfactorily with the blood passing through it, and so reduce the toxæmic condition of the blood, which is probably the important factor in inducing ascites. (2) That the presence of vascular adhesions over the surface of the liver would relieve venous engorgement and so allow a freer supply of arterial blood to the liver. The nutrition of the liver cells would thus be improved and they would be under better conditions to undergo compensatory hyperplasia.

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[*] White, W. Hale: Clinical Journ., April 26, 1899.

[†] Hahn, Nasse, Nencki, and Pawlow: Archiv f. experiment. Path. u. Pharmak., Bd. xxxii, S. 161, 1893.

[‡] Morison: Lancet, 1899, vol. i, p. 1426.

[§] Thomson, H. Campbell: Medico-chirurg. Trans., vol. lxxxiv, p. 265.

[‖] Dickinson, W. H.: Allbutt's System of Medicine, vol. v., p. 691.

[**] Weber, F. P.: St. Bart.'s Hosp. Reports, vol. xxxiv, p. 321.

The compensatory hypertrophy of the liver * will enable the organ to perform more efficiently its important antitoxic functions, and so lead to a latency of the symptoms. If the last hypothesis be true, it is evidently of importance that any operation for the formation of vascular adhesions around the liver should be undertaken before the liver tissue is so disorganised that compensatory hyperplasia is impossible.

Early Performance of Operation Desirable.—It is important that the operation should be done comparatively early and not postponed until the patient is too debilitated to withstand it, for patients with cirrhosis are, at the best of times, far from good subjects. Thus patients may die from peritonitis or from shock immediately after the laparotomy. Another reason for not delaying operative interference is the importance of intervening before the liver tissue is so degenerated that it is unable to undergo compensatory hyperplasia as the result of the improved blood-supply provided by the adhesions. In suitable cases for operation medical measures should only be persisted in while the diagnosis is open to doubt, and they should always be directed to counteract any possible syphilitic disease of the liver. When medical treatment and a course of iodide of potassium have not benefited a case of ascites which is thought to be due to either syphilis or cirrhosis, the question of operative interference should be considered.

When cirrhosis can be diagnosed with fair certainty in the pre-ascitic stage, and when there are evidences of the disease, such as hæmatemesis and splenic enlargement, operative interference has a much better chance than in the late stages.

Results of the Operation.—A large number of cases have been operated upon, and in some instances the operation has been done on cases in which ascites was due to some other cause. Statistics show that no good at all is done in more than half the cases, and that cure occurs only in a small minority.

Up to May, 1902, Greenough † collected 122 cases in which the operation had been done. After deducting 17 in which the disease was not cirrhosis and one case in which the result was not given, there are 104 cases of cirrhosis in which the operation had been performed. Of these, 31 died within thirty days of the operation and 29 were in no way improved, so that 60, or 57 per cent., not only received no real benefit from the treatment, but possibly had their lives shortened; 44, or 42 per cent., were improved, and of these 9 were living and in improved health two years after the operation. This last figure does not include one of Mr. Turner's and my cases operated upon on July 31, 1899, which did not require tapping till March 1, 1902, an interval of more than two and one-half years. In 78 cases collected by Lejars,* death occurred rapidly in 36, in 28 the ascites disappeared, and in 14 notable improvement resulted.

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* It is interesting to note that in a case of hepatic cirrhosis, in which it was suggested that the symptoms were arrested as the result of universal peritoneal adhesions, the liver weighed 89 ounces and presented nodules on its surface which may be interpreted as due to compensatory hyperplasia of the liver cells. The patient died from poisoning by mussels. (F. P. Weber: St. Bartholomew's Hospital Reports, vol. xxxiv, p. 321.)

† Greenough: American Journ. Med. Sciences, vol. cxxiv, p. 979, Dec., 1902.

On the whole, the results are somewhat disappointing, but this may in part be due to the fact that the operation is so often undertaken as a last resource, and late in the course of the disease, when the fatal termination is already near. The earlier the operation is undertaken, the better the chance of improvement or even arrest of the disease. It appears that it does give the patient a chance, as about 10 per cent. are alive and in improved health two years after the operation.

Treatment by Diuretics.—When ascites is small in amount, diuretics may be tried; it is also advisable to give them directly after paracentesis has been performed. It appears, however, that when there is considerable ascitic effusion, diuretics have very little effect, possibly because the renal veins are pressed upon, and from the resulting venous engorgement the kidneys are placed at a disadvantage. For this reason they are often much more effective after paracentesis than before. Diuretics may be tried, but should never be employed to the exclusion of paracentesis.

A large number of diuretics have been employed. A pill containing digitalis, squills, and mercury is one of the most successful diuretics in ascites; the mercury may be in the form of calomel. This pill is called Baillie's pill at St. George's, or Addison's pill at Guy's Hospital. Small doses of calomel may be given not only for their antiseptic action, but also to increase the output of urine, especially when combined with citrate of caffeine. Potassium salts, such as the acetate, nitrate, and bitartrate, are recommended by some, but their diuretic effect is inferior to that of many other available drugs, and the depressing and toxic effect of potassium is a distinct drawback. It is better not to give spirituous solutions, such as spirits of juniper, spiritus ætheris nitrosi, as it is possible they might, like alcoholic drinks, tend to do further damage to the liver.

Copaiba resin in 10 to 15 grain doses has been advocated as a valuable remedy in ascites. It should be given in keratin capsules, which resist the action of the gastric juice, so as to avoid irritation of the stomach. Apocynum is a powerful diuretic, as the name the "vegetable trocar," which has been given to it, implies. It has the disadvantage of irritating the stomach; in order to prevent this, a small dose of cannabis indica should be combined with it. The tincture can be given in 15 to 30 minims three times daily, or the fluid extract (U. S. P.) in 10 minim doses may be employed instead. Musser † speaks encouragingly of its use, but I have been rather disappointed with its effects in the ascites of cirrhosis. Asparagus has often been used as a diuretic. Hare ‡ has seen improvement in ascites of cirrhosis after a drachm of a liquid extract of asparagus given three times daily. Urea, on account of its diuretic action, has also been recommended. I have tried it without any marked effect in several cases, while Goggi has seen bad results follow its administration. Diuretin—a salicylate compound of theobromine—has been tried, but is not of any particular use in the ascites of cirrhosis. Liver substance or extract has been given by the mouth or by subcutaneous injection. Polyuria and diarrhœa result, and ascites may be much diminished. In 14 cases collected by Mouras * ascites disappeared in 7. (*Vide* also Treatment of Cirrhosis.)

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* Lejars: La Semaine Médicale, March 25, 1903, p. 93.

† Musser, J. H.: Journ. Amer. Med. Assoc., Oct. 5, 1901.

‡ Hare, H. A.: Therapeutic Gaz., Oct., 1899.

Treatment by Purgatives.—The ancient treatment of attempting to remove ascites by free purgation has been abandoned, and vigourous drugs like elaterium, gamboge, etc., are no longer given. The excessive diarrhœa thus produced necessarily starves and weakens the patient, while it lessens the urinary excretion and so may tend to induce or increase retention of toxic substances in the blood and lead to toxæmia. Cheadle speaks of cases being "purged to death." Further, violent purgatives readily light up catarrh of the intestine, and so do harm. Repeated small doses of calomel may be given and exert a beneficial antiseptic action as well as clearing out the bowels. Saline purgatives such as sulphate of soda or magnesium may be employed. Jalap powder in one-drachm doses is an effectual purge that may be employed. Turpeth, the Ipomœa turpethum of the Colonial and Indian Pharmacopœias, is recommended in 20 grain doses (Murrell †).

Restriction of Fluid, Etc.—Dickinson ‡ records 6 cases of ascites due to cirrhosis treated by reducing the amount of liquid taken by the mouth down to one pint or less. In two cases the ascites disappeared. In one death occurred two years later from cerebral abscess, and the patient, a boy aged nine years, was found to have a hobnailed liver and universal peritoneal adhesions. The treatment was recommended not as a substitute for tapping, but as an adjuvant. The diminished fluid has distinct disadvantages, since it must tend to produce constipation, thereby increasing fermentation and the tendency to autointoxication. Further, it must curtail the urinary excretion and so tend to favour the onset of toxæmia.

It has recently been urged that the intake of chlorides should be restricted, as they are retained and tend to increase ascites.§

HAEMATEMESIS.

This may be the earliest warning to the individual that he is the subject of any disease more serious than indigestion. Perhaps the most frequent sequence of events is that a man who for years has lived freely and has had a few attacks of gastritis and dyspepsia, due to alcoholic excess, has, while in his usual state of health or after some little initial uneasiness in the stomach or faintness, a copious hæmatemesis.

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* Mouras: Thèse de Paris, 1901, No. 278.
† Murrell: Lancet, 1902, vol. i, p. 1602.
‡ Dickinson: Allbutt's System of Medicine, vol. v, p. 691.
§ Olmer et Audebort: Rev. de Méd., Mars, 1904, p. 199.

Hæmatemesis may be preceded by abdominal discomfort, febrile disturbance, enlarged spleen, and evidence of gastritis. In such cases it is probable that infective gastritis, due to toxic or septic agents, is the exciting cause of the hæmorrhage. The hæmatemesis is sometimes repeated in the course of the next few days, but usually there is a single large hæmatemesis. When hæmatemesis is often repeated the condition is either not cirrhosis, or, if there be hepatic cirrhosis, it is complicated by some factor, such as gastric ulcer, superficial gastric erosions, or ulcerated varicose œsophageal veins, which accounts for the repetition of the hæmorrhages.

Incidence.—Hæmatemesis does not appear from statistics to be so frequent in the course of cirrhosis as is usually imagined. It is such a striking event that it is rather surprising to find that it occurs less often than jaundice and in rather less than one-fourth of all patients dying with a cirrhotic liver.

In 163 cases, obtained by combining Yeld's* (85) and Sears and Lord's† (78) cases, hæmatemesis occurred in 38, or 23.3 per cent.

It naturally occurs rather more frequently in cases who died directly from the effects of cirrhosis, such as ascites, toxæmia, and gastro-intestinal hæmorrhage.

In 80 cases of cirrhosis fatal from the effects of the disease, examined after death at St. George's Hospital, 26, or 32.5 per cent., had had hæmatemesis. In 4 of the 26 cases death was directly due to hæmatemesis. These figures showed that men suffered more frequently than women from hæmatemesis; thus, of 51 men, 19, or 37 per cent., had hæmatemesis, while of the 29 women, only 7, or 14 per cent., had had hæmatemesis.

Hæmatemesis is rare in children. Possibly this may depend on the fact that concomitant alcoholism, which is certainly more frequent in adults, favours extravasation of blood by reducing the coagulability of the blood.

Saunal,‡ however, records fatal hæmorrhage from an œsophageal varicose vein in a girl aged twelve years with cirrhosis. In the Norfolk and Norwich Hospital Museum there is a specimen (No. 59) of dilated œsophageal veins from a girl aged eight years who died after a succession of hæmatemeses. The liver was hobnailed and weighed 36 ounces, the spleen weighed 18 ounces, the skin was slightly tinged, but there was no real jaundice. This case somewhat resembles Banti's disease or cirrhosis supervening in splenic anæmia.

After hæmatemesis the patient is left in a condition of secondary anæmia, the degree of which varies with the amount of blood lost. It is not easy to estimate the amount of blood lost, for though a considerable proportion of it may be vomited up, some always passes into the duodenum and gives rise to melæna, and may thus escape notice, and is necessarily difficult to estimate. After the hæmatemesis the patient sometimes feels relieved and loses any feeling of oppression and heaviness that he may have previously had in the abdomen.

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* Yeld: St. Bartholomew's Hospital Reports, vol. xxxiv, p. 215.
† Sears and Lord: Boston Medical and Surgical Journ. vol. cxlvii, p 285.
‡ Saunal: Thèse de Paris, 1892.

Although hæmatemesis is usually an early symptom of cirrhosis, it may supervene late in the course of the disease, and even prove fatal in a patient with ascites.* This is illustrated by the following case:

> A man aged fifty-four years was admitted under my colleague, Dr. Ewart, into St. George's Hospital in the summer of 1898. He had jaundice, ascites, and albuminuria. Paracentesis to 10½ pints was performed, and after this the fluid did not collect again. He got weaker, and eventually died immediately after a large hæmatemesis. This was the only occasion on which he brought up blood. At the autopsy the liver was cirrhotic and weighed 6 pounds, 10 ounces. The spleen, 10 ounces, the kidneys, 10 ounces each, appeared normal.

The blood is probably generally poured out slowly into the stomach, and thus has time to clot and to be acted upon by the gastric juice and to be mixed with its contents. It is for these reasons darker in colour than the blood in gastric ulcer, which is rapidly extravasated from branches of the gastric arteries. The quantity of blood brought up in cirrhosis is practically always considerable, for the vomiting is chiefly due to the mechanical distension of the stomach by the blood. If only a small quantity is poured out, the blood is not as a rule vomited, but passes into the bowel and gives rise to melæna. This accounts for the fact that melæna may occur without any hæmatemesis in cases of hæmorrhage into the stomach. Occasionally when a small hæmorrhage has taken place, the patient may vomit from some other cause, and a little black or "coffee-ground" vomit may be brought up, but this is somewhat exceptional.

Very large amounts of blood may be vomited in the case of hæmatemesis due to cirrhosis. Thus Osler † refers to a case where 10 pounds were lost in seven days. It is noteworthy that collapse is not so frequent or so marked a symptom as in the hæmatemesis of gastric ulcer, where blood is rapidly poured out. When a varicose œsophageal vein is opened and very large quantities of blood are lost, sometimes at repeated intervals, death may follow, but this does not invalidate the general statement just made that in the ordinary hæmatemesis of cirrhosis, often referred to capillary oozing, alarming symptoms are rare. In fact, sometimes the patients may feel relieved by it.

The temperature after hæmatemesis is subject to some variations. As a rule, it is depressed from shock, but after a few days it becomes normal. It may then remain normal or it may become raised. Fever after hæmatemesis should suggest the existence of some complication, such as tuberculosis, a pleural effusion, especially on the right side, endocarditis, or some septic process in the tonsils, teeth, or elsewhere. Fever may, however, depend on rapidly progressing changes in the liver, especially if the spleen remains enlarged or increases in size. The hæmatemesis and the rapid progress of the cirrhosis may be due to an infection falling on a liver the subject of latent cirrhosis. The hæmatemesis may therefore be followed by fever and ascites may soon develop.

Possibly a slight and transient elevation of temperature after hæmatemesis may depend on the retention in the intestines of a considerable quantity of blood which in decomposing liberates fibrin ferment. This, if absorbed into the circulation, may give rise to an elevation of temperature. Hæmatemesis may act as such a severe shock to a patient who has previously been drinking steadily as to set up the traumatic form of delirium tremens which I have seen prove fatal.

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* H. Fagge: Principles and Practice of Medicine, 1st ed., 1886, vol. ii, p. 134.

† Osler: Practice of Medicine, p. 572, 4th ed.

Etiology of Hæmatemesis in Cirrhosis.—(1) *Gastritis.*—The hæmatemesis may follow a debauch and be due, in part at least, to an exacerbation of a chronic gastritis. In such a case the after-history will indicate whether acute gastritis alone, or whether cirrhosis and gastritis together, were responsible for the hæmorrhage. It is by no means rare to meet with cases of hæmatemesis apparently solely due to gastritis, but in any given case the possibility must be borne in mind that hæmatemesis may after all have been disposed to by a cirrhotic condition of the liver, which subsequently became arrested or latent and gave rise to no further symptoms.

Bad teeth and pyorrhœa alveolaris are not infrequently responsible for infective gastritis, and have often been overlooked in the days before the importance of oral sepsis was recognised. Toxic gastritis may, of course, be set up by a drinking bout. In hæmatemesis from gastritis the blood is thought to be derived by oozing from the capillaries and small veins of the gastric mucous membrane. The hæmorrhage is probably determined by the occurrence of minute areas of necrosis and ulceration in the course of a toxic or septic gastritis. In cases where no source for hæmorrhage can be found in the stomach or œsophagus it may depend on the toxic state of the blood, which shows itself elsewhere by hæmorrhage from the gums, into the skin, etc.

It is unlikely that hæmatemesis is ever due to mere mechanical increase of venous blood-pressure in the walls of the stomach; some inflammatory or degenerate change in the gastric mucosa is a necessary factor. It is, of course, true that often no determining cause is forthcoming; but sometimes fever, gastritis, and splenic enlargement may precede it; Gauthier * suggests that toxines unaltered by the liver act on the intestinal blood-vessels and so set up hæmorrhage.

(2) *Minute Erosions.*—Hæmatemesis in cirrhosis of the liver may be due to minute superficial erosions of the gastric mucous membrane. These, it should be noted, may be easily overlooked, especially as the stomach is blood-stained and somewhat sodden. In order to detect them the stomach should be allowed to remain for some hours in Müller's fluid, after which small erosions will become more evident.

Deguy † has recorded a fatal hæmatemesis in a case of latent cirrhosis with a minute superficial ulceration $\frac{5}{10}$ of a millimetre in size.

Mathieu ‡ has recorded a case of a woman aged thirty who died with hæmatemesis and was thought to be the subject of gastric ulcer; the autopsy showed cirrhosis, varicose œsophageal veins, and numerous hæmorrhagic erosions on the lesser curvature and posterior wall of the stomach. Microscopically there was acute interstitial gastritis, which was the apparent cause of the ulceration.

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* Journn. de Méd., March 10, 1896.

† Deguy: Bull. Soc. Anat. Paris, 1898, p. 767.

‡ Mathieu: La Semaine Médicale, 1897, p. 170.

(3) *Gastric and Duodenal Ulcers.*—Gastric ulcer rarely occurs in patients with cirrhosis of the liver.

In the years 1894–1904 (July) there were 3094 autopsies at St. George's Hospital, among which Mr. T. C. English found that there were 56 cases of gastric ulcer and 19 cases of duodenal ulcer; in two of the 56 gastric cases there was hepatic cirrhosis. According to the Fenwicks,* cirrhosis of the liver is present in 9 per cent. of cases of gastric ulcer.

It is indeed remarkable that gastric ulcer is so comparatively rare in cases of cirrhosis, where the chronic venous obstruction would, by reducing the resistance of the part, tend to render it more vulnerable.

Graham Steele † refers to fatal hæmatemesis from gastric ulcer in a case of cirrhosis.

Duodenal Ulcer.—In rare instances, of which I have seen one, copious hæmatemesis may occur in the course of cirrhosis from a duodenal ulcer. In 184 cases of duodenal ulcer collected by G. M. Cullen,‡ hepatic cirrhosis was present in 2.2 per cent.

(4) *Varicose Œsophageal Veins.*—This is the most important cause of hæmatemesis in cirrhosis, as shown by the fact that it is found to be present in the great majority (80 per cent.) of the fatal cases, where a thorough postmortem examination is made. (Preble.§) In exceptional instances varicose œsophageal veins may be present when the liver is healthy.

Graham and Weir Mitchell‖ have recorded cases of fatal hæmatemesis from this cause in a boy aged seventeen years and in a child where the liver was healthy.

In adults varicosity of the œsophageal veins may be due to chronic alcoholism without any cirrhosis of the liver (Letulle**). It has been thought that this alcoholic phlebectasis is due to the local caustic action of alcohol on the mucous membrane of the œsophagus (G. Muller ††).

In most cases of œsophageal varix the liver is cirrhotic and is responsible for the dilated œsophageal veins in the manner already described. This compensatory collateral circulation serves a useful end in relieving portal engorgement, but, like other compensatory mechanisms, it may fail. Severe hæmorrhage may occur as the result of ulceration of the mucous membrane covering the varices, and may be precipitated by the passage of rough masses of food through the œsophagus. These œsophageal varices and severe hæmorrhages are commoner in association with large than with small cirrhotic livers.

The blood may well up from the œsophagus when the patient is lying quiet in bed, and not be vomited up as it is in gastric ulcer. But in this event the blood does not enter the stomach and will be alkaline. As the varicose œsophageal veins are practically always close to the cardiac orifice, the blood usually runs into the stomach and is vomited up just as in ordinary hæmatemesis.

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* S. and S. Fenwick: Ulcer of the Stomach and Duodenum, p. 76.

† Graham Steele: Medical Chronicle, vol. xix, p. 312.

‡ Cullen: The Scottish Medical and Surgical Journal, vol. i, p. 637, 1897.

§ Preble: American Journ. Med. Sciences, vol. cxix, p. 263.

‖ Graham, Weir Mitchell: Trans. Assoc. American Physicians, vol. xi, p. 215, 1896.

** Letulle: Soc. Méd. des Hôp. Paris, Oct. 24, 1890, p. 783.

†† Muller, G.: Gaz. hebdom. de Méd. et de Chirurg., May 20, 1900.

The loss of blood may be so profuse as to prove fatal. It is probable that nearly all cases of fatal hæmatemesis in cirrhosis are due to ulcerated œsophageal veins.

In Preble's[*] analysis of 60 cases of fatal gastro-intestinal hæmorrhage in cirrhosis the condition of the œsophagus was investigated in 42 and œsophageal varices were present in 35, or 80 per cent. of these cases.

It is highly probable that in many of the cases regarded as due to a general venous oozing, an ulcerated œsophageal varix was overlooked. The ulceration may be very small and may escape notice at the autopsy. Letulle says that the ulcer may only become apparent after the œsophagus has been left for twenty-four hours in Müller's fluid.

The first hæmorrhage may be so profuse as to be immediately fatal. This was so in one-third of Preble's[†] 60 fatal cases of gastro-intestinal hæmorrhage in cirrhosis. In other cases repeated hæmorrhages occur. In rare instances there are considerable intervals of good health between the attacks of hæmatemesis.

Garland[‡] reports a case in which hæmorrhage took place at intervals for seven years and at the postmortem perforation of the dilated veins was found.

Repeated hæmorrhages may occur at brief intervals and kill the patient in a short time from the first symptom of illness, as in a case put on record by Marmasse.[§] In cases of fatal gastro-intestinal hæmorrhage from cirrhosis the primary disease is often latent. The latency of cirrhosis in cases where varicose œsophageal veins are present shows the value of this compensatory mechanism. In only 6 per cent. of 35 cases of cirrhosis in which varices were present were the clinical symptoms characteristic, viz., ascites, enlarged spleen, subcutaneous abdominal veins, etc. (Preble.)

The following case illustrates the latency of cirrhosis until fatal hæmatemesis from an ulcerated œsophageal varix occurs:

A man aged thirty-three years was brought in dead into St. George's Hospital on September 10, 1900, having vomited up a large quantity of blood shortly before death. There were dilated varicose veins at the lower end of the œsophagus, one of which was ulcerated. The veins at the cardiac end of the stomach were somewhat varicose and there was a very minute abrasion of the mucosa over one of them, but the vein, though exposed, was not perforated. The intestines contained blood. There was no ascites. The liver, 4½ pounds, was finely cirrhotic and showed bright yellow nodules, fully justifying Laennec's name, "cirrhosis" (= full of yellowness). Microscopically there was multilobular fibrosis with much fatty degeneration of the liver cells. The gall-bladder contained a small bilirubin-calcium calculus. The spleen, 9½ ounces, was shrunken as if it had been larger.

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[*] Preble: American Journ. of Med. Sciences, vol. cxix, p. 263, March, 1900.
[†] Preble: American Journal of Medical Sciences, vol. cxix, p. 263, March, 1900.
[‡] Garland: Trans. Association of American Physicians, vol. xi, p. 206, 1896.
[§] Marmasse: Bull. Soc. Anat. Paris, 1899, p. 75.

The kidneys, 7½ ounces and 8½ ounces, were hypertrophied but healthy. There was caseous tubercle at the apex of the right lung.

In the following instance death was due to extensive hæmorrhage from an ulcerated œsophageal vein in a patient under treatment for cirrhosis:

Charles W., fifty-one years, a farm labourer, was admitted under my care in St. George's Hospital on September 15, 1900, with slight ascites and œdema of the legs. He had been a moderate drinker, and had never had syphilis. In July, 1900, he had hæmatemesis and melæna; before this he had not suffered from dyspepsia or morning vomiting. He was a weatherbeaten man with a large liver and slight ascites. The spleen was not palpable. There was œdema of the feet, but no neuritis. Pulse 96, low tension, artery tortuous and somewhat atheromatous. Urine 1008, no albumin. He was kept in bed and given milk diet and a mixture containing 15 grains of the iodides of potash, soda, and ammonium three times daily. The œdema of the feet went down and the man's condition improved; he was indeed feeling particularly well, when on September 21 he brought up a quantity of blood from the stomach; he was given suprarenal extract by the mouth and morphia hypodermically; on the next day he again had hæmatemesis and became very blanched, so that concealed hæmorrhage was suspected. He was transfused, but died the same day. At the autopsy there was a small ulcer in the œsophagus, elevated so as to look like a miniature volcano, situated about one inch from the cardiac orifice of the stomach. This opened into a vein; the other veins at the lower end of the œsophagus were not dilated or varicose. The stomach was full of blood clot (25 ounces); the intestines were also filled with blood. The liver, 80 ounces, was pale, finely granular, and intensely cirrhotic; there were numerous hæmorrhagic spots in it. The portal vein was normal. The kidneys were pale but free from arteriosclerotic change. Spleen large. The cavity of the peritoneum contained two pints of ascitic fluid. Testes normal.

(5) *Varicose Gastric Veins.*—Hæmorrhage from varicose veins in the stomach is a very rare event in cirrhosis. Letulle * has described two fatal cases in men aged twenty-three and thirty-nine respectively. Other cases have been recorded by Machiafava,† Hillier, Blake, Jackson, Revillout, Minot.

Hæmorrhage from the Pharynx.—Bouchard ‡ has pointed out that small nævi are frequently present at the back of the pharynx and that hæmorrhage from these nævi may give rise to hæmatemesis. The pharynx of cirrhotic patients with hæmatemesis should therefore be carefully examined, as the cause of the hæmorrhage, if found, can be satisfactorily treated by local styptics.

It has thus been seen that hæmatemesis in cirrhosis may occur (i) when there is no morbid lesion visible to the naked eye except gastritis. (ii) From small superficial abrasions of the gastric mucous membrane. (iii) In very rare instances from gastric or duodenal ulcer. (iv) From rupture or ulceration of varicose veins at the lower end of the œsophagus; this is the most important cause. (v) From ulcerated varicose veins in the stomach. (vi) From the pharynx, the blood being swallowed and subsequently vomited.

Diagnosis of Hæmatemesis of Hepatic Cirrhosis from that Due to Other Causes.—Without mentioning all the possible causes of hæmatemesis it will be useful to refer to those causes that are common and therefore most likely to be confused with hepatic cirrhosis.

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* Letulle: La Presse Médicale, Nov. 29, 1898.

† Machiafava: Boll. delle Soc. Lancisiana, Rome, 1898

‡ Bouchard: Rev de Méd., Oct., 1902, p. 837.

(A) Gastric ulcer in men of mature years runs a very chronic course, gives rise to continued pain and dyspepsia, but very rarely goes on to perforation. In some cases that I have seen there was an absence of tenderness on palpation, although the ulcer, as verified at the autopsy, was large and adherent to adjacent parts. Hæmorrhage from the stomach in these cases may give rise to a suspicion of cirrhosis. When, as sometimes occurs, a patient with entirely latent cirrhosis dies from very copious hæmatemesis, due to rupture of varicose veins at the lower end of the œsophagus, it is impossible to diagnose the condition from gastric ulcer except on the greater probability of cirrhosis giving rise to hæmatemesis in a middle-aged man than gastric ulcer.

The occurrence of repeated hæmorrhages and painful dyspepsia are against cirrhosis. If the spleen is palpable, the diagnosis is against gastric ulcer. In young women gastric ulcer is far more frequent than cirrhosis. When cirrhosis occurs in them, there is usually considerable enlargement of the liver and spleen and distinct evidence of alcoholic excess. Pressure over the gastric ulcer in young women gives rise to sharp pain, compared by the patient to that of a knife; this is quite different from the diffuse tenderness elicited on deep pressure in gastritis accompanying cirrhosis. The character of the blood in hæmatemesis due to cirrhosis is a point of some importance. It is black from the more prolonged stay in the stomach and is often clotted, forming masses that may stick in the patient's pharynx. In gastric ulcer the blood is poured out more rapidly from a leaking artery, and is therefore brighter, more arterial, less acted upon by the gastric juice, and not necessarily coagulated.

(B) From pore-like erosions of the gastric arteries. Very free and repeated hæmorrhages may take place from minute erosions. In these cases there is no deep tenderness and there is a comparative absence of antecedent gastric symptoms. Attention has recently been drawn to these cases by Dieulafoy * and Steven.† It is important to recognise them, since the proper treatment is to perform laparotomy, open the stomach, and suture the bleeding point. The chief distinction from the hæmatemesis of cirrhosis seems to be the frequency of repeated and copious hæmatemesis in a patient who has none of the signs, symptoms, or history of portal cirrhosis.

(C) In carcinoma of the stomach the vomited blood is black, resembles "coffee-grounds," and is usually small in quantity, so that melæna is not noticed. In carcinoma of the pylorus hæmatemesis is in rare instances profuse; in such cases the stomach will probably be dilated and a tumor may be palpable. As a rule, carcinoma of the stomach is accompanied by so much pain and the vomited blood is so small in amount that the condition is not likely to imitate cirrhosis. If tested, the vomit

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* Dieulafoy: (Exulceratio simplex.) La Presse Médicale, Jan. 19, 1898.

† Steven, J. L.: (Pore-like Erosions of the Gastric Arteries.) Glasgow Med Journ., vol. li, p. 5, Jan., 1899

will probably be found not to contain hydrochloric acid. Another important point in the diagnosis of gastric carcinoma is the presence of a tumor near or at the umbilicus, in the line of the falciform ligament, or on the surface of the liver.

(D) Periodic hæmatemesis may occur for years in *splenic anæmia;* sometimes there is very fair health in between the attacks; in some instances recurrent hæmorrhages have occurred over a period of ten years. The anæmia is more marked and the splenic enlargement more considerable than in cirrhosis. A correct diagnosis from cirrhosis depends largely on this fact, and is of importance inasmuch as splenectomy appears, from Osler's * and Harris and Herzog's † observations, to offer the best chance of cure. These cases usually occur in men between thirty and forty years of age, and so might easily be regarded as due to latent cirrhosis.

Closely allied to chronic splenic anæmia of adults, and probably a late development or complication of that disease, is the condition described by Banti, and often spoken of as Banti's disease. Splenic anæmia is after some years complicated by secondary cirrhosis of the liver and jaundice. In this condition severe gastro-intestinal hæmorrhages may occur.

In leukæmia, hæmatemesis and melæna may occur and be associated with both splenic and hepatic enlargement; the diagnosis from cirrhosis depends on an examination of the blood.

Prognosis.—Hæmatemesis is rarely fatal in cirrhosis; in 80 cases where cirrhosis was the direct cause of death hæmatemesis was the sole cause in only 4, or 5 per cent.

Treatment of Hæmatemesis from Cirrhosis.—The patient should be kept perfectly quiet in bed and for three or four days nothing whatever should be given by the mouth. Ice should certainly not be sucked, as an indefinite quantity of water is thus taken, which necessarily sets up peristaltic contractions of the stomach, and so may give rise to fresh hæmatemesis, while, further, the cold water must abstract a considerable amount of heat from the patient, who is often already somewhat collapsed. Thirst, which is often a cause of distress to the patients, is a natural result of the loss of blood and of the draining of the tissues to replace the fluid part of the blood. The mouth should be cleaned by pads of moistened cotton-wool and enemata of warm water should be given every four hours to relieve thirst. If necessary, subcutaneous transfusion with saline solution may be employed. In order to insure rest a hypodermic injection of morphia is useful; this calms the natural mental disturbance and anxiety of a person who has unexpectedly brought up blood.

The administration of digitalis or digitalin, ergot, lead, or other drugs which constrict the vessels and raise blood-pressure, is useless if not dangerous. Nitrite of amyl, which dilates the small blood-vessels and lowers blood-pressure, has more theoretical grounds in its favour, but has not been used in the treatment of hæmatemesis. Chloride of calcium increases the coagulating power of the blood, and so may lead to thrombosis in the vessels responsible for the hæmorrhage. It may be given in a dose of a drachm per rectum in the enemata of water given to relieve thirst, and may be repeated if hæmatemesis recurs and the patient's life is threatened from anæmia and exhaustion. As recurrent hæmatemesis in cirrhosis is usually due to ulceration of varicose veins at the lower end of the œsophagus, it is advisable to try and act locally on the bleeding area by the administration of Ruspini's styptic, which is largely composed of gallic acid; the styptic may be given in half to one drachm doses in an ounce of water by the mouth. Two successive half-drachm doses may be given.

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* Osler: Trans. Assoc. American Physicians, vol. xvii, 1902.

† Harris and Herzog: Annals of Surgery vol. xxxiv, p. 111, July, 1901.

The various preparations of suprarenal gland substance may also be given by the mouth in recurrent hæmatemesis so as to obtain the local vasoconstrictive effect on the bleeding vessels. It should not be given hypodermically or per rectum, as, its general effect on blood-pressure being to raise the tension, it would, if absorbed into the general circulation, tend to increase hæmorrhage from any leaking vessel. Another remedy which may be given by the mouth is turpentine in twenty minim doses in spirits of chloroform (♏x) and water (℥j) every four or six hours.

The local application of an ice-bag to the abdomen is recommended by some writers, but its effect is open to some doubt, and, on the whole, it is better to do without it.

If there is great collapse after hæmatemesis, transfusion of normal saline solution subcutaneously or into the veins should be performed.

The lower bowel should be cleared out by a soap-and-water or by a glycerin enema, or when there is no recurrence of hæmorrhage and there is any abdominal distension or slight fever, a blue pill followed by a saline draught containing sulphate of magnesia should be given on the third day. During the first three days it is better to give nothing by the mouth, rectal injections of water (10 to 20 ounces) being given to relieve thirst every four or six hours as seems necessary. Nutrient enemata or suppositories may also be given every six hours, but in many instances this is not really necessary, and the patient is more comfortable without. In fact, the mental influence of nutrient enemata is often more valuable than their physical effect.

If there is nothing to suggest gastric ulcer, cautious feeding by the mouth may usually be begun after the third day, provided there has been no return of hæmatemesis. Peptonized milk or peptonized milk gruel should first be given and the diet gradually improved. After a week or ten days, according to his general condition, the patient should be allowed to get up.

A most important point is the after-treatment, which consists in a light, simple diet, abstinence from alcoholic stimulants and from highly spiced and stimulating articles of food. The importance of change of life should be clearly and carefully explained to the patient, and he should be advised to become a total abstainer.

When, as sometimes happens, hæmatemesis occurs in patients with ascites, removal of the fluid by paracentesis may be followed by a cessation of hæmatemesis. In such cases congestion may be aggravated by the intra-abdominal pressure of ascites.

HAEMORRHAGE FROM THE BOWEL.

Hæmorrhage from the bowel is a frequent symptom in cirrhosis. It may be divided into (i) melæna as ordinarily understood, viz., blood so altered that it is darkened in colour by the action of sulphuretted hydrogen on the iron of the hæmoglobin, and by other factors, such as the effect of the secretions of the alimentary canal on the blood; (ii) hæmorrhage from piles or from the mucous membrane of the rectum, the blood being more or less of its normal colour.

Melæna (ἡ μελαινα νοσος, "the black disease") commonly accompanies or follows hæmatemesis. The blood, which, by distending, mechanically irritates the stomach, is expelled in two directions—into the œsophagus and into the duodenum. In other words, while hæmatemesis is going on the patient vomits into the duodenum. The hæmoglobin of some of the blood-corpuscles is acted upon by the gastric juice and reduced to acid hæmatin; there is hardly sufficient time for this to take place in the mass of the blood that is driven into the duodenum, so that the blackness and tarry appearance of the motions are largely the result of the iron of the hæmoglobin being acted upon by sulphuretted hydrogen in the intestines and converted into some compound containing sulphide of iron.

Melæna from gastric hæmorrhage may occur without concomitant hæmatemesis. This depends on the fact that the stomach is not overdistended by the blood poured out into it. When the volume of blood poured out into the stomach is small, it will pass into the duodenum mixed with the contents of the stomach and appear in the motions. In such cases the fact that melæna has occurred may escape observation or only be found out accidentally, and may then be regarded as due to a latent duodenal or intestinal ulcer. It may be difficult or impossible to diagnose the source with certainty in the absence of other signs of cirrhosis. In duodenal ulcer there should be deep tenderness in the situation of the duodenum and pain two or three hours after food. Duodenal ulcer may complicate cirrhosis and give rise to melæna without hæmatemesis. I have seen one case in a man aged forty years in which this coincidence was present. The duodenal ulcer, undiagnosed during life, gave rise to very acute pain in the right loin.

Melæna in cirrhosis may depend on hæmorrhages of considerable size from the mucosa of the intestines. This event is analogous to the gastric hæmorrhages, and is related in a similar fashion to the abnormal conditions of the portal circulation and to the inflamed and altered state of the mucous membrane of the intestine. Melæna in cirrhosis is usually seen about the same time as hæmatemesis, viz., in the pre-ascitic stage, but it may occur after ascites has come and gone, and be a terminal phenomenon.

In the following cases extensive hæmorrhage from the rectum immediately preceded death:

A woman of alcoholic habits, aged forty-nine, under my care in St George's Hospital, was tapped for ascites twice within a fortnight after admission. After this she lived for seven and one-half weeks in an extremely drowsy condition, but did not again become ascitic. The day before her death she passed two pints of blood from the bowel. There were no subcutaneous hæmorrhages at any time. At the autopsy the mucous membrane of the lower 6 inches of the rectum was inflamed, and though no definite ulcer could be found, the rectum must have been the source of the hæmorrhage; for no blood or blood staining was found higher up in the bowel. The liver was cirrhotic.

In a man aged forty-four years death was immediately preceded by melæna. He had twice been tapped for ascites due to cirrhosis; his case is referred to elsewhere (p. 274), as he had successively hæmaturia, epistaxis, and lastly melæna.

Melæna of slight degree may occur from small multiple hæmorrhages taking place from the mucosa of the intestines and due to hepatic insufficiency. These extravasations are analogous to the multiple hæmorrhage occurring under similar conditions into the skin and other tissues.

Piles occasionally occur in cirrhosis and may give rise to some bleeding. It is certainly remarkable that piles are not more common in cirrhosis, as it would naturally have been expected that portal obstruction would almost constantly lead to a varicose condition of the hæmorrhoidal veins. Frerichs,* Sappey, Thierfelder, Nothnagel,† and others are all agreed on the comparative rarity of piles in cirrhosis. It has been thought that hæmorrhage from piles in cirrhosis serves a useful purpose by relieving hepatic engorgement, and that their cure by operation may be followed by hæmatemesis or by advance in the downward course of the disease; in other words, that piles in cirrhosis is a condition that it is dangerous to cure.

Treatment of Melæna.—For considerable melæna without any hæmatemesis a turpentine enema may be given. The patient should be kept quiet and, if necessary, given morphia. If bleeding occurs from piles, the local condition should be attended to.

HAEMOPTYSIS.

Hæmoptysis in the course of cirrhosis is somewhat infrequent. When it does occur, it is usually comparatively slight in amount. It may be due to various causes:

1. *False Hæmoptysis.*—This may depend on epistaxis from the posterior nares, or on hæmorrhage from the mucous membrane of the naso-pharynx. These hæmorrhages are not uncommon in the late stages of the disease and may be due to the general toxæmic state. Bouchard ‡ has insisted on the frequency of nævi in the pharynx, from which hæmorrhage may occur independently of grave toxæmia.

2. *Hæmorrhage from the larynx* may be due to concomitant tuberculous disease, or to venous oozing depending on hepatic insufficiency.

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* Frerichs: Diseases of Liver, vol. ii, p. 47. Transl. New Sydenham Soc.

† Nothnagel: Diseases of Intestines. English translation, p. 298.

‡ Bouchard: Rev. de Méd., Oct., 1902.

Dreyfuss observed a bleeding tumor in the larynx of a patient with cirrhosis.

3. *Hæmorrhage from the lungs* due to (*a*) pulmonary tuberculosis; (*b*) extreme congestion accompanying pulmonary collapse secondary to abdominal distension; (*c*) venous oozing depending on hepatic insufficiency.

The occurrence of hæmoptysis in patients with cirrhosis should always arouse a strong suspicion of pulmonary tuberculosis. It is, however, not always justified. In an alcoholic woman under my care who said she had had slight hæmoptysis for years, the lungs showed no trace of tubercle at the autopsy.

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Galliard: Union Médicale, Nov., 1889.
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Dieulafoy: Manuel de Interne. Path., t. ii, 689 (Larynx).

EPISTAXIS.

Bleeding from the nose is by no means an infrequent symptom of cirrhosis. It may be part of the general tendency to hæmorrhage depending on hepatic insufficiency, but it may supervene before there is any other evidence of this toxæmia or be the first sign of this complication. It occurs from one nostril—usually, as was pointed out long ago, from the right. It usually comes from a point near the anterior extremity of the septum which can be easily compressed (Bouchard *). The hæmorrhage may be due to ulceration of an arterial nævus, and may if uncontrolled be so severe as to lead to syncope. Relapses are very prone to occur. In a patient of Dieulafoy's † repeated hæmorrhages occurred from an ulcerated nævus in the nostrils.

Epistaxis may alternate with hæmorrhages from other sources.

In a case under my care a man aged forty-four had first hæmaturia, then epistaxis, and just before death melæna. His liver was markedly cirrhotic and had given rise to ascites, which had been tapped twice.

HAEMORRHAGES FROM OTHER SITUATIONS.

Hæmaturia may occur from hepatic insufficiency and be comparable to epistaxis, but it is rare.

In a man aged fifty years who was under my care in 1903, with cirrhosis, transient hæmaturia occurred at the same time as epistaxis and oozing from the gums.

The following case is of interest as an example of hæmaturia and other forms of hæmorrhage.

Cirrhosis. Hæmaturia due to Nephritis. Epistaxis. Fatal Melæna.—A man aged forty-four, of alcoholic habits, was admitted to St. George's Hospital under my care on June 20, 1900, with swelling of the abdomen, flatulence, pain near the umbilicus, swelling of the legs, and loss of flesh and strength dating from an attack of pneumonia eighteen months previously. He had the signs of cirrhosis with a large liver, but had very distinct hæmaturia with casts and a sp. gr. of 1009. The question arose whether it was a case of cirrhosis with intercurrent nephritis or one of primary malignant disease of the kidney with secondary growths in the liver. There were no hæmorrhages elsewhere in the body and there was nothing to show that the hæmaturia was due to hepatic insufficiency. The abdomen manifestly contained fluid and required tapping twice With rest in bed the hæmaturia passed away, but the patient's general condition got worse. On July 9 there was only a trace of albumin, and on July 11 none at all. On July 11 and 12 he had epistaxis, and on the latter day rapidly become comatose; though he revived a little after transfusion, he died on July 14 with considerable melæna. At the autopsy the liver, 68 ounces, was cirrhotic and finely granular; the portal vein was free from any thrombosis. The kidneys weighed 7½ and 8 ounces each, and showed parenchymatous nephritis. The mucous membrane of the small intestine was pigmented, the change being more marked near the stomach. The spleen weighed 10 ounces.

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* Bouchard: Rev. de Méd., Oct., 1902, p. 837.

† Dieulafoy: Manuel de Intern. Pathologie, t. ii, p. 669, 1901.

Menorrhagia and Metrorrhagia.—In the early stages of cirrhosis metrorrhagia is often seen; very possibly this is partly connected with chronic alcoholism. In the later stages of cirrhosis there is usually amenorrhœa, though when hepatic insufficiency supervenes, hæmorrhages may occur from the uterine mucous membrane.

The occasional formation of a *hæmatoma in the rectus abdominis muscle* has already been referred to as a possible evil effect of the collateral circulation in connexion with the veins in the round ligament. (*Vide* p. 213.)

In a case recorded by Lefas* in which portal cirrhosis was complicated by jaundice and grave toxæmia (icterus gravis) the cause of the hæmatoma was thought to be fatty degeneration of the endothelium of the intramuscular capillaries.

General Hæmorrhages.—In the late stages of cirrhosis when the liver has become incapable of stopping poisons absorbed from the alimentary canal, a condition of hepatic toxæmia results. The blood-vessels suffer and hæmorrhages may occur from their damaged walls all over the body. The general hæmorrhagic condition may in some instances be due to hæmic infection. Thus in a remarkable case of cirrhosis with hæmorrhagic bullæ Monnier† cultivated Bacillus coli and streptococci. In such cases there is naturally some fever. Petechial hæmorrhages into the skin are frequent, while hæmorrhages are often seen from the mucous membrane of the mouth, blood oozing from the gums or from cracks on the dry dorsum of the tongue. The sordes thus produced give rise to an offensive odour of the breath.

In an exceptional case recorded by Webber‡ hæmorrhage took place from the external ears, in addition to hæmoptysis and bleeding from the gums. Leudet§ also reports hæmorrhage from the external ear in cirrhosis.

In the following case thrombosis and hæmorrhages were combined. These two conditions are usually associated with opposite conditions of the blood as regards coagulation, the blood coagulating more rapidly in thrombosis and less rapidly than normal in hæmorrhage.

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* Lefas: Bull. Soc. Anat. Paris, 1902, p. 586.
† Monnier: Compt. rend. Soc. de biol., 1896, p. 65.
‡ Webber: Lancet, 1894, vol. i, p. 1000.
§ Leudet: Ann. Mal. de l'or, Oct., 1890

An alcoholic woman aged forty years was admitted under my care in March, 1900, for severe hæmatemesis thought to be due to cirrhosis; in two days' time she developed typical delirium tremens, from which she recovered under the administration of hyoscine $\frac{1}{75}$ gr. subcutem. After her recovery from delirium she had numerous hæmorrhages all over the body; it was noticeable that there were several small thrombosed veins in the neighbourhood of some large cutaneous hæmorrhages. There were thrombosed veins on the front of the abdomen, on the right mamma, and right arm. The veins of the legs were not affected.

The treatment of hæmorrhages is partly local and partly general; the local treatment consists in the application of remedies such as adrenalin to bleeding spots where they can be reached, while the general treatment consists in giving chloride of calcium in half-drachm doses three times a day for six doses, and in attempting to reduce the general toxæmia by getting the kidneys to act with citrate of caffeine, etc., draughts of water, etc. The bowels should be kept open, and subcutaneous transfusion may be employed if it is thought necessary.

NERVOUS SYMPTOMS.

A considerable number of nervous manifestations may occur in the course of cirrhosis; as a rule the more striking are noticed late in the disease and are associated with advanced toxæmia. The slighter nervous symptoms, such as headache, giddiness, muscular weakness and tremor, disturbance of mental power, disordered sensation, pruritus, may occur earlier in the course of cirrhosis. It may not be easy to determine satisfactorily in every case whether symptoms supervening in cirrhosis are solely due to the liver and its functional failure, or whether they depend on other factors, such as alcoholic excess or renal disease, or whether the symptoms are the outcome of hepatic inadequacy combined with one of these additional factors. Thus, delirium tremens is due to recent alcoholic excess, while other forms of delirium may be most satisfactorily explained as due to hepatic or renal inadequacy. As long as the kidneys excrete toxic bodies which the liver fails to stop, the patient may remain fairly free from marked nervous symptoms, but headache, mental torpor, and depression are readily produced by food which has no bad effects in a healthy person. Failure in the excretion of urine gives rise to increased toxæmia and often precedes the development of acute nervous phenomena.

Slight mental disturbance is common in patients with cirrhosis, but it is natural to ascribe loss of memory, failure of will-power and of intellectual ability, solely or in part to the effects of alcohol. As in other morbid conditions of the liver, mental depression and hypochondriasis are common. Muscular tremor is not infrequent and is often largely alcoholic and due to sleeplessness or to nights disturbed by nightmares and bad dreams.

Pruritus.—Itching of the skin is a symptom of hepatic inadequacy and depends on the failure of the liver cells to arrest poisons manufactured in the alimentary canal. It is more often associated with jaundice, but may occur in its absence; it is not a common symptom, and when it does occur is usually seen late in the course of the disease.

Hanot * speaks of a case where it occurred, and was persistent, a year before symptoms of cirrhosis developed, without any jaundice.

The more severe nervous symptoms include coma, delirium, convulsions, paralysis, and contractions. It has been thought by some that a large cirrhotic liver is more prone to be associated with grave nervous symptoms, but there is probably not enough to justify a very definite statement as to this relationship.

Coma.—Cases of cirrhosis which run their full course usually die with coma, which often comes on when ascites has disappeared (post-ascitic stage) or is stationary and small in amount. Coma is due to grave toxæmia, which may be purely hepatic and depend on the destruction of the hepatic cells being so widespread that the liver fails to stop poisons manufactured in the alimentary canal, as a result of which the circulation becomes flooded with them. If the kidneys are active, the poisons may be got rid of, but in many cases coma is precipitated by failure in the excretory activity of the kidneys. Though coma is more commonly a terminal phenomenon, it may be transitory and be removed by treatment. I have several times seen coma disappear as the result of intravenous transfusion; the same result may follow bleeding. A patient in a drowsy, semi-comatose condition may wake up sufficiently to try and get out of bed and then relapse into a state of coma. Before coma comes on there may be extreme irritability and restlessness, due to toxæmia and resembling that seen in renal toxæmia or uræmia.

Delirium may be terminal and precede coma, or more rarely it may temporarily supervene in the course of the disease and disappear. In the case of transient delirium it must be borne in mind that delirium tremens not uncommonly occurs in the course of cirrhosis. I have seen short bouts of fever associated with delirium lasting two days or so, recur in a patient with cirrhosis before ascites developed. The character of the delirium varies; usually it is of a low wandering type, but occasionally it is very violent and requires considerable restraint; the patient may get out of bed or attempt to do so. The character of the delirium may change, or quiet and noisy phases may alternate.

Delirium tremens may occur under different circumstances in the course of cirrhosis. It may come on in the usual way from continued drinking in a patient with latent cirrhosis, or even when the disease has advanced into the stage of ascites. It may come on after hæmatemesis, and then be more of the nature of traumatic delirium † and comparable to the delirium which is precipitated, so to speak, by a fractured thigh or pneumonia in an alcoholic subject. In other cases where hæmatemesis is not very profuse, a mild form of delirium tremens may develop and may possibly be due to the treatment—viz., deprivation of food by the mouth for a few days.

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* Hanot: Archiv. Général. de Méd., vol. clxxvii, p. 67.
† Compare S. West: Clinical Journal, vol. vii, p. 58.

Convulsions are sometimes seen at the close of the disease. Delirium often passes into coma, and convulsions may be added shortly before death.

Paralysis.—In addition to paraplegia due to peripheral neuritis of alcoholic origin, it occasionally happens that paralysis complicates cases of cirrhosis. Cerebral hæmorrhage or thrombosis may occur in a patient with cirrhosis of the liver, but usually when the cirrhosis is latent. In very rare instances hemiplegia occurs in patients with cirrhosis and no gross change is forthcoming to account for it.

In an alcoholic woman aged fifty-three who was under my care in St. George's Hospital with cirrhosis, right hemiplegia and aphasia developed so as to suggest cerebral hæmorrhage. At the autopsy no naked-eye morbid change could be found in the brain. The liver was markedly cirrhotic (weight, 70 ounces).

Levi * fully records terminal coma and facial paralysis in a man aged seventy with an alcoholic history and cirrhosis and without any cerebral change except œdema.

It is possible that cirrhosis might dispose to cerebral hæmorrhage by producing a hæmorrhagic tendency. I have seen one case of cirrhosis in a girl aged nine years in whom there were multiple cerebral hæmorrhages, fever, and probably a terminal infection. It has been thought that thrombosis in the cerebral vessels may be disposed to by hepatic cirrhosis under certain conditions.

In a girl aged twelve years hemiplegia was found to be due to thrombosis of the cerebral veins. There was ascites due to hepatic cirrhosis and it was thought by Fisher † that the thrombosis depended on absorption of organic bodies from the peritoneal cavity.

In children with multilobular cirrhosis there are in exceptional cases marked nervous symptoms suggesting juvenile general paralysis; very possibly there are examples of parasyphilitic cirrhosis combined with general paralysis of the insane.

Dr. Ormerod ‡ has given a full description of a case that I often saw when I was house physician at St. Bartholomew's Hospital. Cirrhosis of the liver was never suspected during life, the symptoms being progressive paralysis, loss of mental power going on to idiocy, fever, and marked emaciation. He referred to three cases, all in one family, that had been described by Gowers § as examples of "tetanoid chorea," and to three cases, also in one family, recorded by Homén ‖ and regarded as due to inherited syphilis.

DURATION.

Portal cirrhosis commonly lasts a considerable time; one, two, or more years usually intervene between the appearance of symptoms due to the liver, if indeed their first appearance can be accurately determined, and the termination of the case; while the progress of the lesion in the liver may become arrested, and from compensatory changes the disease may become latent. Sometimes, however, the disease runs a very rapid course; in such cases there are a certain amount of fever, pain in the abdomen on the right side, enlargement and tenderness of the liver, œdema of the legs, hæmorrhages, and the early development of ascites. These cases are more often seen in comparatively young subjects, who have been drinking heavily, and may run their course in two to six months (Hanot *). When cirrhosis runs a very rapid course, degenerative changes take place in the liver cells and the condition is complicated by a process much the same as that underlying icterus gravis, only less acute.

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* Levi: Archiv. Général. de Méd., vol. clxxviii, p. 165.

† Fisher, T.: Lancet, 1901, vol. ii, p. 845.

‡ Ormerod, J. A.: St. Bartholomew's Hosp. Reports, vol. xxvi, p. 57, 1890.

§ Gowers: Diseases of Nervous System, Ed. 1, vol. ii, p. 656.

‖ Homén: Neurologisches Centralblatt, 1890, p. 514.

TERMINATION AND METHOD OF DEATH.

As has been pointed out (p. 226), cirrhosis may be latent owing to compensation having been effected. The compensatory anastomosis of the œsophageal veins with the gastric veins may be a source of danger, and sometimes very profuse and even fatal hæmatemesis may result from ulceration or rupture of an œsophageal varix. In such cases cirrhosis may be quite unsuspected, although the fatal issue is a direct result of hepatic cirrhosis.

In only 6 per cent. of 35 cases of hæmatemesis from œsophageal veins were the cases typical of cirrhosis from a clinical point of view (Preble †).

Hæmatemesis is rarely directly fatal, but Preble has collected 60 cases of fatal gastro-intestinal hæmorrhage in cirrhosis. In 80 cases fatal from the direct effects of cirrhosis examined at St. George's Hospital, 4, or 5 per cent., only were due to hæmatemesis. Death may occur after a single large hæmorrhage or after a series of repeated hæmorrhages. In a third of the cases collected by Preble death followed a single hæmorrhage.

In patients with cirrhosis, which has not yet produced ascites, death may be due to a number of complications (*vide* p. 281), which frequently throw any symptoms due to cirrhosis into the shade. These complications are in some instances the results of alcoholism; thus, there can be little doubt that the influence of alcoholism is responsible in great measure for the frequency with which tuberculosis, peripheral neuritis, and cardiac failure appear as complications of hepatic cirrhosis. Tuberculosis is extremely frequent in the course of cirrhosis, and not uncommonly cirrhosis of the liver is discovered after death in a patient dying from phthisis. Generalized tuberculosis may carry off a patient with cirrhosis long before loss of flesh and impairment of general nutrition have appeared. I have several times seen generalised tuberculosis in fat patients with cirrhosis.

When chronic renal disease is associated with cirrhosis of the liver, the clinical aspect is mainly that of kidney disease, and death usually results from uræmia, which, it may be noted, is very much like the late toxæmic stage of cirrhosis.

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* Hanot, V.: Archiv. Général. de Méd., June and July, 1892.

† Preble: American Journ. of the Medical Sciences, vol. cxix, p. 263.

Acute infections, such as erysipelas and pneumonia, when they occur in the subjects of cirrhosis, are extremely likely to lead to a fatal termination. It has been said that acute infections of this kind are more fatal in portal cirrhosis than in hypertrophic biliary cirrhosis, since the liver cells are in a better state of preservation in the latter disease. Occasionally acute infection may fall on the liver itself and set up acute degenerative changes in the liver cells, and so give rise to symptoms resembling those of acute yellow atrophy. But inasmuch as the liver is not healthy previous to the acute infection, as is the case in acute yellow atrophy, it is perhaps more convenient to speak of the condition as icterus gravis. An acute infection may attack the smaller bile-ducts without affecting the liver cells to such a degree as to produce acute yellow atrophy, though the clinical resemblance is considerable. In this connexion the following case is of interest:

An alcoholic waiter at a well-known club, aged forty-seven, had had hæmatemesis seven weeks before death; ascites, jaundice, and œdema of the feet subsequently developed; he was admitted into St. George's Hospital and was tapped; he remained jaundiced, and for the last three weeks of his life was delirious. The liver weighed 60 ounces and showed multilobular and monolobular cirrhosis, with inflammation of the small bile-ducts, which contained inspissated masses of bile-stained material or microscopic calculi. The spleen weighed 10 ounces and was soft. Probably an acute secondary infection was implanted on the top of old-standing common cirrhosis and especially involved the bile-ducts.

When ascites has developed death usually follows before the patient requires tapping more than once, or at the most twice. Indeed, if paracentesis has to be repeated several times, the case is either complicated with some degree of chronic peritonitis or is not one of cirrhosis at all. After one or two tappings the fluid may not reaccumulate and the patient may linger on for a time in a drowsy and very feeble condition—a post-ascitic stage. Death is usually due to increasing weakness and coma. There is often low, muttering delirium; active delirium is rare, but I have known it to be maniacal. More often the patient becomes more and more insensible and passes into deep coma. Occasionally while in this toxæmic state death may be precipitated by profuse hæmorrhages from the stomach or rectum.

When ascites has developed death may be due to some complication such as acute peritonitis; in rare instances this is due to the introduction of infection by the trocar; but it occurs independently of tapping, and is then due to infection from within, either by the blood-stream or in rare instances from some lesion, such as tuberculous ulceration of the intestines, which allows micro-organisms to pass into the peritoneal cavity. Acute infections, such as pneumonia and erysipelas, may also attack and cause the death of a patient with ascites due to cirrhosis.

From a degenerated and fatty condition of the heart muscle sudden death may occur; this is by no means common in my experience, but in 53 fatal cases of cirrhosis Cheadle * found that death occurred suddenly

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* Cheadle, W. B.: Some Cirrhoses of the Liver, p. 51.

in this way in 6. More often a patient dies slowly with a failing heart but in a general toxæmic condition.

COMPLICATIONS.

Tuberculosis.—The liability of patients suffering from cirrhosis to be affected with tuberculosis of the lungs and peritoneum has been already referred to under the heading of morbid anatomy, where statistics were given.

In about 12 to 14 per cent. of cases with cirrhosis death is directly due to pulmonary tuberculosis; in many of these cases the cirrhosis is latent and is only discovered after death. In other instances pulmonary tuberculosis may escape detection or only show itself by very few signs. Tuberculous peritonitis may not be suspected, as the ascites is very naturally regarded as due to cirrhosis. In tuberculous peritonitis supervening in cirrhosis there may be more abdominal pain than in ordinary ascites, and if tapping be performed, the fluid is found of a higher specific gravity (1020) than in ordinary cirrhosis (1010) and turbid.

In the following case ascites was due to tuberculous peritonitis supervening in the course of cirrhosis:

A fat woman, aged forty-nine, of a marked alcoholic aspect, was admitted under my care at St. George's Hospital on January 9, 1902, with ascites, œdema of the feet, altered and blunted sensation in the legs, and bronchitis. The liver was enlarged, the breath very foul, and there was morning sickness. She was treated as a case of cirrhosis, and on January 17 the abdomen was tapped; the fluid was turbid and of a specific gravity of 1020; owing to the thickness of the abdominal wall it was difficult to get a trocar sufficiently long to reach the peritoneal cavity and only about a pint of fluid was withdrawn. Death occurred on January 19. At the autopsy the liver (68 ounces) was markedly cirrhotic and microscopically contained much fat; the spleen weighed 12½ ounces. There were some chronic peritonitis and recent generalized tuberculous peritonitis. There was an old tubercle at the apices and much bronchitis in the lower lobes of both lungs.

Generalised Tuberculosis.—In cirrhosis the possibility of generalised tuberculosis should be thought of when there is continued fever and the patient rapidly goes down-hill without any appreciable ascites. Generalised tuberculosis may prove fatal in patients comparatively fat.

Bronchitis.—Some degree of bronchitis is not uncommon in cirrhosis and may be an accidental accompaniment. On the other hand, it may be directly related to the cirrhosis, and may be due to collapse of the bases of the lungs from upward displacement and impaired movement of the diaphragm due to ascites, flatulence, or an enlarged liver. It may be part of a general catarrh from alcoholic excess or be the result of backward pressure from a failing heart. Since what appears to be bronchitis may be really rapid pulmonary tuberculosis, it is advisable to test the sputum for tubercle bacilli in cases of bronchitis in cirrhosis.

In the following case rapid tuberculosis gave rise to the signs of general bronchitis.

A fat alcoholic man, aged fifty, who had had delirium tremens, was under my care for a few days in St. George's Hospital in March, 1900. He had œdema of the feet and a hæmorrhagic eruption on the legs, a dilated heart, a large liver, and general bronchitis; the sputum contained a little blood. The urine (1020) was free from albumin. He was thought to have cirrhosis of the liver and backward pressure from cardiac dilatation, with possibly a pulmonary apoplexy. After being in for three days, with delirium at night, he quite suddenly died. At the autopsy the liver (108 ounces) showed multilobular cirrhosis with much fatty change; the left lobe overlapped the spleen, which weighed 28 ounces. The kidneys weighed 9 ounces each and were healthy. There was no ascites. There was a pint of clear fluid in each pleural cavity and very dense adhesions at both apices. There were small cavities at both apices and recent firm caseous masses in the lower lobes and miliary tubercles throughout both lungs. There was no pulmonary apoplexy. There was bronchitis and tuberculous ulceration of the larynx. The heart (17 ounces) showed fatty infiltration and degeneration and was dilated, but was free from valvular disease. Examination of the lungs showed tubercle bacilli.

Pleurisy with Effusion.—Pleurisy is not uncommon in the course of cirrhosis and is often a manifestation of concomitant pulmonary tuberculosis. It is more frequent on the right side, and this is very probably due, as suggested by Villani,* to a spread of inflammation or infection from the liver through the diaphragm. The pleurisy may be acute and accompanied by pain and fever, or of an indolent and chronic character. In the latter case the condition is much like a hydrothorax, but, as already mentioned, it is often tuberculous in origin.

James † records a curious case of ascites and right pleural effusion in which a communication was thought to exist between the right pleura and the peritoneal cavity, inasmuch as tapping the pleura emptied the abdomen, and, in fact, seemed to be more effectual than paracentesis abdominis.

The fluid may be serous, serofibrinous, or in rare cases hæmorrhagic. Hæmorrhagic pleurisy is rare in cirrhosis. It is usually due to tuberculosis (Barjon and Henry,‡ Jean §), though it is possible that in some instances it may be due to hepatic insufficiency, and so resemble the petechiæ and general hæmorrhages seen in the late stages. In some instances it has been suggested that the hæmorrhagic character of the pleural effusion is due to alcoholism. (Fernet.‖) A pleural effusion, especially on the right side, is more likely to be hæmorrhagic than a concomitant ascites. The following case illustrates the relationship of tuberculosis and a hæmorrhagic pleural effusion:

A man, aged forty-nine, died in St. George's Hospital with cirrhosis of the liver and tuberculosis. At the autopsy there was a pleural effusion on both sides—serous on the right side, hæmorrhagic on the left side; there were numerous tubercles in the lung on the side of the hæmorrhagic effusion.

In the following case the hæmorrhagic character of the pleural effusion probably depended on traumatism:

A billiard marker, aged forty-three, was admitted under my care with fever, a large right-sided pleural effusion, enlargement of the liver, and ascites. The effusion was twice tapped, and clear fluid was drawn off on both occasions, which contained neither tubercle bacilli nor pneumococci. He passed into a toxæmic condition, and although transfused, died without any improvement. His abdomen never required tapping. The right pleura contained much dark blood-stained fluid; the lung was collapsed and covered with lymph, which was hæmorrhagic in one place and suggested that the blood had come from a newly formed vessel; there was a little obsolete tubercle at the apex. There was serous ascites, no chronic peritonitis, a multilobular cirrhotic liver weighing 65 ounces, with small bilirubin-calcium calculi in the gall-bladder. The round ligament contained a big vein the size of the little finger. (*Vide* Fig. 32.)

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* Villani: Rif. Med., Rome, March 9, 1895.

† James: Trans. Medico-chirurg. Soc., Edinburgh, vol. xviii, p. 191, 1898–99.

‡ Barjon et Henry: (Lyon Médical, June 19, 1898.)

§ Jean: Thèse, Paris, 1891.

‖ Fernet: Bull. de la Soc. Med. des Hôp., June 22, 1900, p. 781.

Taylor* records a case of hæmorrhagic pleural effusion which was independent of tuberculosis and probably due to an acute septic infection.

The presence of a right-sided pleural effusion in a doubtful case is in favour of cirrhosis, as against simple thrombosis of the portal vein, since it does not occur in the latter condition unless complicated by cirrhosis. It should, however, be borne in mind that some degree of dulness on percussion, loss of vocal vibrations and of breath sounds at the right base, may be due to upward projection of a large cirrhotic liver, or to a smaller cirrhotic liver being pushed up by ascites, and not to any pleural effusion. In the same way friction at the right base may be due to local peritonitis and not to pleurisy.

Peripheral Neuritis.—The early symptoms of peripheral neuritis are so often thrown into the shade by the ascites or other effects of cirrhosis on which attention is focussed that the minor degrees of neuritis probably often pass undetected. Cramps, muscular tenderness, and loss of knee-jerk are not uncommon in cases of cirrhosis admitted for ascites or hæmatemesis, and are, generally speaking, to be referred to alcoholism. Alcoholic neuritis is commoner in women and is often associated with pulmonary tuberculosis; in such cases the liver is sometimes cirrhotic and nearly always fatty; but the clinical picture is, in the main, that of neuritis, not of hepatic disorder.

The terminal stages of cirrhosis are marked by symptoms due to hepatic insufficiency, such as epistaxis and other hæmorrhages, delirium, and coma. The toxic coëfficient of the urine will, if the kidneys be healthy, become increased as a result of the liver failing in its antitoxic function of destroying or neutralizing toxic bodies emanating from the portal system. Hence a toxæmic neuritis may occur in the late stages of cirrhosis as the result of hepatic insufficiency. If alcohol has been taken freely up to the onset of the neuritis, it must then be considered to be alcoholic in origin, but when the absence of this cause can be established, hepatic insufficiency with resulting toxæmia is a satisfactory explanation.

In a case of Gouget's† neuritis came on two weeks before death in a woman previously of alcoholic habits, who, however, had not had any stimulant for the two months that she had been in hospital. The arms and legs were simultaneously affected, which is unusual in the alcoholic form. It is interesting to note that Hayem observed the same type of neuritis in a case of primary carcinoma of the liver.

Delirium tremens, another complication of cirrhosis, has been dealt with on page 277.

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* Taylor, F.: Guy's Hospital Reports, vol. lii, 1896.

† Quoted in Levi's Paris Thèse, 1896.

The occurrence of **chronic peritonitis** in the bodies of patients dying with cirrhosis of the liver is referred to elsewhere (p. 222). The importance of realising that chronic peritonitis may exist in cases of cirrhosis is that ascites thus produced may frequently recur and last much longer than in cases of cirrhosis uncomplicated by chronic peritonitis, where ascites is a close forerunner of death. As a result of chronic peritonitis the omentum may become rolled up and form a firm mass running across the abdomen.

In a case, recorded by Benham,* of cirrhosis complicated by chronic peritonitis the omentum and mesentery were so thickened and matted together that they formed a pulsating mass during life.

Renal Disease.—The occurrence of albuminuria in cirrhosis (*vide* p. 232), and the morbid lesions of the kidney (*vide* p. 221) that may occur, have been dealt with elsewhere. Here the clinical aspect of cases where the two conditions are combined will be referred to. *A priori* it would naturally be expected that death would occur earlier in cirrhosis complicated by renal disease than in ordinary cases of cirrhosis, inasmuch as the toxæmia depending on hepatic inadequacy would not be obviated by the excretion of toxic bodies by the kidneys. This hypothesis, however, is not supported by statistics. Both in Yeld's † figures from St. Bartholomew's Hospital and in the cases at St. George's Hospital the average age of patients dying with the combined conditions was higher than in those patients who succumbed to uncomplicated cirrhosis of the liver. When the two diseases are met with in the same person, the clinical symptoms are rather renal than hepatic. This is in accord with the hypothesis that in the combined condition the toxæmia would be more marked.

Gout not unnaturally is met with in the past history of some patients who come under observation with the symptoms of cirrhosis. It is, however, very rare to see frank attacks of gout in patients with symptoms of active cirrhosis. A large liver, which may in some instances be due to early or latent cirrhosis, is not infrequent in gouty subjects.

In 44 cases of cirrhosis tabulated by Yeld ‡ the joints were healthy in 34 and contained uratic deposit in 9, or 21 per cent. In 5 of the nine cases the kidneys were granular.

Secondary or Terminal Infections.—Towards the end of cases of cirrhosis secondary infections are far from uncommon. Probably the bactericidal power of the blood is diminished in the same way that it is in chronic heart and kidney disease, and as a result infection is more likely to occur. The peritoneum is disposed to infection by chronic congestion, often by some chronic peritonitis and ascites, while paracentesis may be the immediate cause of infection. Suppurative or fibrinous peritonitis is not a very uncommon termination to a case; and, as already pointed out, tuberculous peritonitis may supervene in the course of cirrhosis.

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* Benham, F. L.: Trans. Clin. Soc., vol. xxviii, p. 226.

† Yeld, R. A.: St. Bartholomew's Hospital Reports, vol. xxxiv, p. 226.

‡ Yeld: St. Bartholomew's Hospital Reports, vol. xxxiv, p. 215.

Secondary infection of the liver itself, giving rise to acute degeneration of the liver cells and to icterus gravis, may occur. Cases have been recorded by Pitt * (4), Weber,† and others, and are probably not very infrequent. Erysipelas, pericarditis, pneumonia, infective endocarditis, are also occasionally met with.

In 65 fatal cases of infective endocarditis tabulated by Kelynack ‡ cirrhosis was found in 4.

In a case of cirrhosis of the liver Councilman § found a secondary infection with streptococci giving rise to purulent infiltration of the retroperitoneal glands, thrombosis of iliac veins and inferior vena cava, with secondary embolic infarcts in the lungs.

The museum of St. Bartholomew's Hospital contains an interesting specimen (2295 h) of a spleen containing a mass of laminated blood-clot the size of an orange from a man who had cirrhosis of the liver and streptococcal endocarditis of the aortic valves.

Thrombosis.—Thrombosis is rare in the course of cirrhosis. Thrombosis of the portal vein when it occurs is most frequently associated with cirrhosis, but it only occurred in 10, or 3.3 per cent., of 334 cases of cirrhosis examined after death at St. Bartholomew's Hospital. (Langdon Brown. ‖) I have seen severe phlebitis of the leg develop in the late stages of cirrhosis. A case of multiple thrombosis and hæmorrhages was referred to on page 276.

DIAGNOSIS.

The history of dyspepsia, often associated with evidences of alcoholic excess and of considerable duration, hæmatemesis which cannot be explained satisfactorily on other grounds, and enlargement of the liver and spleen, are the broad lines on which the disease can be diagnosed in the preascitic stage. The development of ascites in a patient who has manifested the above symptoms and is, in addition, more or less cachectic leaves little room for doubt that a late stage of cirrhosis has been reached.

THE DIFFERENTIAL DIAGNOSIS.

The diagnosis of cirrhosis from other conditions has already been partially dealt with under the heads of ascites and hæmatemesis. The diseases which simulate cirrhosis, in so far as the production of ascites and of gastro-intestinal hæmorrhage are concerned, such as chronic peritonitis, in which is included perihepatitis, and gastric ulcer, have thus been dealt with.

From Hypertrophic Biliary Cirrhosis with Chronic Jaundice.—Portal and hypertrophic biliary cirrhosis, though distinct types, may in certain instances be combined, while other cases show a transition from one to the other. It may be pointed out that exactly the same blending of distinct types is seen in the case of kidney disease. Chronic parenchymatous nephritis, which may be compared to hypertrophic biliary cirrhosis, and the granular (arteriosclerotic) kidney, which may be likened to portal cirrhosis, may overlap, run into each other, or be combined.

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* Pitt, G. N.: Trans. Path. Soc., vol. xl, p. 351.

† Weber, F. P.: Trans. Path. Soc., vol. l, p. 136.

‡ Kelynack: Encyclopædia Medica, vol. iv, p. 365.

§ Councilman, W. T.: Trans. Assoc. American Physicians, vol. xi, p. 213, 1896.

‖ Langdon Brown: St. Bartholomew's Hospital Reports, vol. xxxvii, p. 62.

The clinical and anatomical features of the diseases may both be found in the same person; thus, in hypertrophic biliary cirrhosis a secondary portal cirrhosis frequently develops before death, and the patient, who has for years presented the symptoms and signs of biliary cirrhosis, dies with ascites and perhaps gastro-intestinal hæmorrhage. Cases of portal cirrhosis with a large liver and rather persistent, intercurrent jaundice occasionally occur and very closely imitate hypertrophic biliary cirrhosis; the distinction between the two depends on the jaundice not being permanent, in the slighter degree of splenic enlargement, and on the occurrence of ascites or other characteristic evidences in portal cirrhosis. In cases of portal cirrhosis which run an acute course, or where more acute inflammatory changes supervene on portal cirrhosis of some standing and affect the bile-ducts, the clinical and anatomical features may show a combination of biliary and portal cirrhosis.

From Other Enlargements of the Liver.—A patient may come under observation, say for examination for life insurance or for digestive disturbance, and be found to have an enlarged liver without any other manifestations of cirrhosis. The question then arises whether there is latent cirrhosis or some other morbid change in the liver. If there is proof or history of alcoholic excess, the enlargement may be due to fatty change, to early or to latent cirrhosis, or to temporary engorgement. If the organ is smooth, free from tenderness and pain, and the spleen is not palpably enlarged, the probabilities are in favour of fatty enlargement. Tenderness is in favour of engorgement or of early cirrhosis; enlargement of the spleen points to cirrhosis or to malarial hepatitis with engorgement.

Malarial Enlargement.—As a result of chronic and severe malarial infection very considerable enlargement of the liver with tenderness on palpation results. This is combined with splenic enlargement and usually with irregular fever. The patient is much run down in health and weight and the condition presented is very like that of early but advancing cirrhosis. The history that the patient, often a young man and not specially alcoholic, has been the subject of continued malaria abroad is important. These cases often improve very rapidly under treatment in England, and the enlargement of the liver is much diminished or disappears entirely.

Chronic Venous Engorgement.—The enlarged liver due to the backward pressure of obstructive heart or lung disease may imitate a cirrhotic liver; especially as there is not infrequently a transient systolic apical murmur in cirrhosis. In forming a diagnosis the history and appearance of the patient and the presence of other signs of cirrhosis or of heart disease are important. Thus alcoholism, hæmatemesis and an enlarged spleen point to cirrhosis, while rheumatic fever in the past, hæmoptysis, and beneficial results from digitalis and strophanthus, are in favour of chronic venous engorgement.

In **leukæmia** the liver is often greatly enlarged, and epistaxis and hæmatemesis may occur. In the myelogenic variety the spleen is very greatly enlarged, while in the chronic lymphatic form the superficial lymphatic glands are enlarged. The diagnosis is easily made by examination of the blood.

From Carcinoma of the Liver.—In the late stages of cirrhosis when the patient is cachectic and ascites and jaundice are both present, the resemblance to malignant disease may be very close. Enlarged glands above the clavicle, if present, are strongly in favour of carcinoma. The history of the patient, revealing chronic alcoholism and a considerable period of ill health from long-continued dyspepsia, suggests cirrhosis. In many instances doubt must exist until the abdomen is tapped and the liver can be thoroughly palpated.* If it is small, it is probably cirrhotic; if large and smooth, it might be either cirrhosis or massive cancer growing inside the organ, but the former is much more probable, both because primary cancer is rarer and because it need not give rise to either ascites or jaundice. Enlargement of the liver with multiple umbilicated nodules points to malignant disease.

A hydatid cyst deeply embedded in the substance of the liver expands the affected lobe, makes it prominent, firm, and enlarged, usually in a downward direction. In cirrhosis the enlargement is more uniform, affecting both lobes, while the surface is more or less irregular. It must, however, be remembered that when a large hydatid destroys a considerable amount of liver substance, compensatory hyperplasia of the other lobe may occur, and that the resulting enlargement may appear uniform, as in cirrhosis. A large cirrhotic liver, unless displaced forward by a flatulent stomach, which is only a temporary condition, or by some other cause, an event not often met with, is not nearly so prominent as in hydatid disease. In hydatid the general health is good, while in cirrhosis there is usually some impairment, or signs of chronic alcoholism.

Syphilitic Disease of the Liver.—A past history of syphilitic infection or manifest lesions elsewhere in the body would point to this explanation of an enlarged liver. In syphilitic disease of the liver the organ is often irregularly enlarged, whereas the two lobes of the liver are generally uniformly affected in latent cirrhosis. Pain is more frequent in syphilitic disease, and albuminuria, if present, is of diagnostic value as pointing to the probable existence of lardaceous disease. Sometimes all external manifestations of syphilis are wanting and the only clinical evidence forthcoming is diminution of the enlarged liver under a tentative use of iodides. The difficulty of distinguishing between the two conditions may be so great that a patient with cirrhosis should always be treated with iodides for a time.

In **splenic anæmia,** where recurrent attacks of hæmatemesis are often met with, the splenic enlargement and the anæmia are more marked than in cirrhosis, and there is usually a diminution in the number of white blood-corpuscles, or leucopenia. The diagnosis between splenic anæmia and portal cirrhosis is a rather delicate and difficult matter, since, on the one hand, splenic anæmia may terminate in cirrhosis of the liver (Banti's disease), while, on the other hand, both hæmatemesis and ascites may occur in cases of splenic anæmia where fibrosis of the liver is absent, as shown after death. Splenic anæmia with periodic hæmatemesis is chiefly distinguished from portal cirrhosis by the greater degree of anæmia and of splenic enlargement.

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* Compare Landrieux: Journ. des Praticiens, Nov. 25, 1899, p. 737.

Intra-hepatic Suppuration.—In acute cases of cirrhosis accompanied by fever and considerable enlargement of the liver the question of distinguishing between it and intra-hepatic suppuration might present some difficulties. Hæmatemesis and an alcoholic history point in favour of cirrhosis, while a hectic temperature, localized hepatic tenderness, leucocytosis, and a history of residence abroad and dysentery, or of conditions, such as recent appendicitis, suppurating piles, or gall-stones, which might lead to pylephlebitis or to suppurative cholangitis, are in favour of intra-hepatic suppuration.

Carrington * has described the case of a woman who had an enlarged liver and a temperature oscillating between 98.4° and 104°; pylephlebitis was diagnosed, but after death the liver weighed 72 ounces and showed rapidly progressing cirrhotic changes and a fatty condition of the liver cells.

Typhoid Fever.—In acute cases of cirrhosis with a raised temperature there may be considerable resemblance to typhoid fever. In patients who have been drinking heavily and present an enlarged liver and spleen, raised temperature, and diarrhœa, a rapid diagnosis from typhoid fever is sometimes only possible by means of the agglutination test (Widal's reaction). In children with a raised temperature, diarrhœa, and swollen abdomen the suspicion of a perforating typhoid ulcer has even arisen. A case in point was referred to on page 219.

Intestinal Obstruction.—Strange though it may seem, intestinal obstruction has been suspected in a patient with repeated vomiting from alcoholic gastritis and abdominal distension from ascites. Careful examination of the patient's history and general condition should, however, correct a first impression of this kind and lead to appropriate treatment for the pressing gastric symptoms.

A man aged fifty-two with ascites and abdominal distension was admitted under me in St. George's Hospital on January 11, 1902. He had been thought before admission to be suffering from acute intestinal obstruction, and had, indeed, been seen in consultation by my colleague, Mr. Sheild, who recognised that the condition was cirrhosis of the liver and recommended him to the hospital for medical treatment.

It may be pointed out that intestinal obstruction might conceivably occur from strangulation by a band of peritoneal adhesions in connexion with perihepatitis, and that, of course, intestinal obstruction may occur in a patient with cirrhosis.

Treves † quotes Lusseau's ‡ case of cirrhosis in which the third part of the duodenum was compressed by a cicatricial band.

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* Carrington: Guy's Hospital Reports, Series iii, vol. xxvii, 1884.
† Treves: Intestinal Obstruction, p. 446, 2d ed., 1899.
‡ Lusseau: Progrès Médical, 1879, p. 545.

PROGNOSIS.

The prognosis depends in great measure on the reparative power of the body and on its ability to compensate for the lesions of cirrhosis. Some discussion on the compensatory mechanism is therefore necessary in order to get a clear idea of the problems involved in the prognosis of cirrhosis.

The organism attempts to compensate for the evil effects of cirrhosis in two ways: (I) By a further development of the anastomosis which normally exists between the tributaries of the portal vein and the general systemic veins. (*Vide* p. 209.) (II) By compensatory hyperplasia of the liver cells.

(I) The dilatation of the communications between the tributaries of the portal vein and the general systemic veins compensates for the mechanical obstruction to the passage of portal blood through the cirrhotic liver. It thus relieves the engorgement of the portal area, and should thereby tend to obviate hæmatemesis, and probably to delay the development of ascites and possibly to assist in its removal.

If the effects of hepatic cirrhosis were chiefly mechanical and due to venous engorgement of the portal area, the more extensively the portal vein was put into communication with the inferior vena cava, the better would be the result. But a most important element in the pathological results of cirrhosis is the destruction of the liver cells and the necessary loss of their various functions, or hepatic insufficiency. One of the most important of these functions is the antitoxic action, or the power of stopping poisons absorbed from the alimentary canal and preventing their entry into the general circulation.

If, therefore, this collateral circulation be carried to its logical extreme, namely, by making the portal vein open directly into the inferior vena cava or Eck's fistula, so that the portal circulation is short-circuited and the liver is virtually put outside the circulation, the results, as obtained by Hahn, Nasse, Nencki, and Pawlow * on dogs, are very striking. The symptoms were much like those of uræmia; the urine contained carbamic acid, which is normally changed by the liver into urea. Similar symptoms were produced by carbamic acid, and hence it was regarded as the cause of the toxic manifestations resembling those of uræmia.

It is therefore probable that the good effects of the collateral circulation in cirrhosis are not purely mechanical. Possibly diversion of some of the blood from the liver relieves congestion of that organ and so enables it to deal more satisfactorily with the remaining blood that still passes to it. It is also conceivable that the state of nutrition of the organ is improved by relieving the congestion of the portal vein, and that it is thus able not only to be more active functionally, but to undergo compensatory hyperplasia to greater effect. This subject was also dealt with in considering the way in which the Talma-Morison operation for the relief of ascites does good. (*Vide* p. 258.)

The second anatomical change by which an attempt is made to compensate for the evil effects of cirrhosis is compensatory multiplication of the liver cells. (*Vide* p. 208.) As a result of compensatory hyperplasia the liver increases in size. This attempt at compensation in cirrhosis is very general, but its success is very variable. In many instances the effort at compensation in cirrhosis is in vain. Though for a time it staves off the evil day and the disease remains latent, there is always the danger that the cirrhotic process may spread to the hyperplastic areas and that they may become engulfed like the rest of the liver; further, the vigourous nodules of adenomatous liver tissue may outgrow their nutrition and undergo necrosis; or they may undergo fatty degeneration from some general cause, as fever (action of toxines), for example, in the nodular cirrhosis sometimes seen in tuberculosis, or extensive hæmorrhage may take place into the substance of the liver from the dilated vessels and bring the compensation to a premature end.

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* Hahn, Nasse, Nencki, and Pawlow: Archiv f. experiment. Path. u. Pharmak., Bd. xxxii, p. 161, 1893.

In some instances the compensation is sufficiently good to restore a fair equilibrium, and the disease is latent so long that it may be thought to be almost cured. There is hardly a return to perfect health, for there is a want of reserve power, and the compensation, if strained, may give way. The importance of this compensatory hyperplasia is well expressed in Hanot's axiom that while the diagnosis of hepatic cirrhosis is made from the state of the connective tissues, the prognosis depends on the condition of the hepatic cells.

Period of the Disease.—In ordinary cirrhosis the prognosis is, generally speaking, gloomy, but there are several special points which must be taken into consideration. Thus the prognosis is necessarily different at an early and at a late period of the disease. It is quite possible for the earliest symptom of importance—hæmatemesis—to be succeeded by many years of life, and even for the cirrhosis, which gave rise to it, to remain permanently latent.

It should be remembered that though the disease may become latent and remain so for years, the condition is not one of real cure. The morbid change in the liver, though compensated for, is still there, and may be restarted, or the compensatory mechanisms may fail. Thus fatal hæmorrhage may occur from dilated and varicose œsophageal veins, or, as just mentioned, fibrosis and fatty degeneration may involve the areas of hyperplastic liver cells. It has been pointed out several times that the prognosis in the late stages is very bad, and that ascites due to cirrhosis uncomplicated by chronic peritonitis is usually followed by death within a short time. A drowsy, sleepy condition points to a general toxæmia, and though it may be temporarily removed by treatment, it is prone to recur and pass into coma, and is therefore an extremely grave sign.

The **effect of treatment** of course has an important bearing on the prognosis; not so much in any attempt to remove the fibrous tissue in the liver, for drugs such as iodide of potassium and chloride of ammonium are useless in ordinary cirrhosis, but from the point of view of preventing any further aggravation of the disease. Cutting off all alcohol is a most important step, and on the patient's power of will to abstain his future will to a great extent depend.

It may be pointed out that very marked improvement under iodides makes the prognosis good because it tends to alter the diagnosis of portal cirrhosis into that of syphilitic disease of the liver.

General Nutrition.—It is hardly necessary to insist on the importance of the patient's general state of nutrition as a factor in the prognosis. A well-nourished patient has naturally a much better prospect than an emaciated subject. The appearance of the face, haggard and sunken about the eyes and temporal fossæ in cases which are rapidly going down-hill, is an instinctively recognised guide in forming a very grave prognosis, while the nutrition of the skin elsewhere, and of the muscular development generally, is of considerable value. The presence of stigmata on the face has been said to be of bad prognosis, but as an isolated manifestation this has seemed to me of little value; a dirty, earthy tint of the skin is more significant of a general nutritional change.

Age has some influence on the prognosis. Thus, Cheadle * found that the average age of 37 cases in which temporary or prolonged improvement occurred was thirty-nine years, or nearly ten years less than the average age of fatal cases of cirrhosis. It is possible that in these cases the cirrhosis developed rapidly as the result of heavy drinking, and that the process was not so far advanced as in older subjects where the fibrosis has slowly developed. A comparatively early age is a favourable factor, inasmuch as the general nutrition is probably fairly preserved, and that, as a result, reparative and compensatory processes can be carried out in an efficient manner.

Size of the Liver.—From what has been said about compensatory hyperplasia it is theoretically probable that enlargement of the liver improves the prognosis, since it is more likely to be associated with latency of the disease than a small one. In practice this is hardly reliable as a hard-and-fast rule, since enlargement may be temporary and due to alcoholic excess, to absorption of poisonous products from the alimentary canal, or to complications such as cardiac failure and backward venous pressure. Further, in the early stage when the cirrhotic process is actively advancing the liver is considerably enlarged. But in the absence of constitutional symptoms, complications, or other signs that the disease is active and progressive, the outlook is better in a case of cirrhosis with an enlarged than with a small liver.

This is borne out by the fact (*vide* p. 199) that the liver is larger in persons affected with cirrhosis but dying from accident or from independent diseases than in patients dying directly from the effects of the disease. Most of the cases of cirrhosis reported as recoveries have enlarged livers. According to Hanot and Gilbert † and Cheadle, ‡ two-thirds of the cases conform to this statement. Cheadle dealt with no less than 30 cases in which recovery, either temporary or prolonged, resulted after tapping.

Enlargement of the spleen is present in progressive cases and is absent, as a rule, in latent cases in which compensation has taken place.

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* Cheadle: Some Cirrhoses of the Liver, p. 72.

† Hanot et Gilbert: Soc. Méd. des Hôp., May 27, 1890.

‡ Cheadle: Some Cirrhoses of the Liver, p. 69.

Its size is, therefore, an indication of some value, and in cases thought to be latent, splenic enlargement should suggest the possibility of approaching hæmatemesis, ascites, or toxæmic manifestations. It should be regarded as a danger-signal and as an indication for purgation by which portal engorgement and intestinal fermentation can be diminished or obviated. If the spleen remain enlarged after hæmatemesis, the possibility of a recurrence or of the near advent of ascites should be borne in mind.

Hæmatemesis is usually an early symptom; often, indeed, the first indication to the patient that he has anything serious the matter with him. In such cases the immediate prognosis is usually good, for the patient recovers, and may by a careful life escape any further manifestations of cirrhosis for years, or possibly forever. Hæmatemesis is rarely fatal, but when it is so, the first hæmatemesis is usually followed by death. When hæmatemesis is frequently repeated at short intervals it is probably due to an ulcerated œsophageal vein, and the prognosis is worse than in the ordinary single hæmatemesis, as the patient may die from anæmia and exhaustion. When hæmatemesis occurs in patients with ascites, the prognosis is even more gloomy than it was before, as the occurrence of hæmatemesis makes it probable that the ascites is due to cirrhosis of the liver and not to concomitant chronic peritonitis.

Multiple or general hæmorrhages, from the gums, throat, nose, skin, etc., make the prognosis very grave, as they point to an advanced degree of toxæmia, which may be succeeded by coma.

When **ascites** has developed, the patient's days are, as a rule, already numbered. According to Hale White,* indeed, cases of uncomplicated cirrhosis, *i. e.*, without chronic peritonitis, never survive to be tapped more than once. Though this may not be strictly in accord with general impression, and though recovery after paracentesis has often occurred in cases where the existence of cirrhosis has subsequently been established after death from other causes, the great gravity of ascites due to cirrhosis can hardly be overestimated.

While insisting on the extreme gravity of ascites due to cirrhosis, it may be pointed out that it is a late phenomenon in the disease, and probably a manifestation of an advanced degree of toxæmia. But the development of ascites in a patient thought to have cirrhosis must not be regarded as necessarily the equivalent of a death warrant. Many cases have been recorded where recovery has occurred after paracentesis for ascites thought to be due to cirrhosis. (Bristowe,† Millard,‡ and Cheadle,§ and many others.)

An instructive case is mentioned by Hawkins‖ of a man who had been a hard drinker and was under the late Dr. Murchison in St. Thomas' Hospital with ascites. After this he became a total abstainer and lived in fair health for twelve years. At his death from pericarditis and granular kidneys the liver was found to weigh

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* Hale White: Guy's Hospital Reports, vol. xlix, p. 1, 1892.
† Bristowe: Trans. Med. Soc., 1892, p. 271.
‡ Millard: Bull. et mem. Soc. Méd. d. Hôp., 1892, p. 153.
§ Cheadle: Some Cirrhoses of the Liver, p. 69.
‖ Hawkins, H. P.: Allbutt's System, vol. iv, p. 180.

59 ounces, its capsule was much thickened and adherent to the diaphragm, and on section it showed multilobular cirrhosis. Ehret * reports the details of a man who thirty years before his death, which was due to carcinoma of the esophagus at the age of seventy-two, had jaundice, ascites requiring several tappings, and pain over the liver and spleen; he became temperate. The liver was small and cirrhotic, the spleen large and surrounded by firm adhesions.

When, as in Hawkins' case, death subsequently occurs from some other cause, and the diagnosis of cirrhosis is confirmed, we must conclude that the compensatory mechanism is sufficient to explain the cure. This event is also well illustrated by cases of laparotomy for the cure of ascites due to cirrhosis by means of the production of artificial peritoneal adhesions.

It must be remembered that ascites may be associated with cirrhosis, but due to some concomitant cause, such as chronic peritonitis or mitral disease. In such cases death is less likely to supervene rapidly than in cases where there is no cause for ascites other than cirrhosis. When ascites is due to chronic peritonitis, repeated tappings may be required, and the outlook as regards prolongation of life is better than when ascites is solely due to cirrhosis.

A point of interest is how much chronic peritonitis will give rise to associated ascites in cirrhosis; it certainly need not be universal.

If in a case thought to be cirrhosis the ascitic effusion is loculated from the presence of adhesions, it is probable that for this reason the prognosis is better than in cases where there are no grounds to suspect adhesions. But, on the other hand, it is difficult to be certain that cases of loculated or encysted ascites are not entirely due to chronic peritonitis, to the exclusion of cirrhosis.

Œdema of the legs in the course of cirrhosis is, apart from any local cause, of bad omen, for it either points to a general toxæmic state or is associated with and is possibly due to pressure of the ascitic exudation on the inferior vena cava. In either of these conditions the outlook is extremely bad.

Functional activity of the kidneys, or renal permeability, is an important factor in the prognosis, and the urine should always be measured and examined, so that any feature in its amount and in its solid contents may be at once detected and treated. So long as the kidneys remove the toxic bodies which the cirrhotic liver allows to pass into the general circulation, the patient is in a fairly satisfactory state; but failure in the urinary excretion brings on a condition of hepatic toxæmia which resembles uræmia. The presence of diacetic acid, as shown by the appearance of a port-wine colour on the addition of ferric chloride, in the urine makes the prognosis very grave, as acid intoxication is imminent and may lead to coma.

Fever.—A raised temperature is met with in cases which run a comparatively acute course, or when some complication such as tuberculosis is present, and is therefore of bad prognosis.

Complications, such as pulmonary tuberculosis, peripheral neuritis, etc., make the prognosis graver. When a granular kidney is found associated with cirrhosis, the age at death is, as shown by statistics, higher than in cases fatal from uncomplicated cirrhosis, and clinically the renal symptoms are more prominent. It need hardly be added that any of the acute infections, such as peritonitis, pericarditis, erysipelas, or pneumonia, necessarily make the outlook extremely bad.

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* Ehret: München. med. Wochen., 1903, S. 321.

The integrity of the hepatic cells is of great importance in recovery from erysipelas (Roger and Garnier *). In ordinary cirrhosis where the cells are much affected erysipelas is usually fatal. Ten cases of ordinary cirrhosis attacked with erysipelas all terminated fatally (Bridiers de Villemor †), whereas in hypertrophic biliary cirrhosis, where the liver cells may remain intact and actively functional, recovery may be hoped for.

TREATMENT.

The important subject of treatment may be considered under the following heads:

1. To prevent any further advance in the morbid change in the liver. This includes abstinence from alcohol, careful dieting, and special attention to the condition of the alimentary canal so as to prevent or minimise fermentation and autointoxication. In the early pre-ascitic stage of cirrhosis these measures may be spoken of as prophylactic.

2. The palliative or symptomatic treatment. The treatment of conditions such as hæmatemesis and ascites will be found under those headings.

3. To promote the compensatory mechanisms by means of which the disease becomes latent.

1. TO PREVENT AND REMOVE FACTORS WHICH FAVOUR THE MORBID CHANGE IN THE LIVER.

Irritating or toxic substances, such as alcoholic drinks, spicy or stimulating food, must be avoided. Alcohol must be entirely prohibited throughout the treatment of the disease, and care should be taken not to give the patient alcohol in his medicines. Thus, tinctures, alcoholic extracts, and spirituous solutions, such as spiritus chloroformi, should be avoided and infusions or watery extracts substituted. If it is impossible to prevent the patient taking some stimulant, a relaxation of his strict duty to the patient, the medical attendant should see that it is taken after meals and largely diluted. On a patient's power of will to become a rigid and total abstainer his future will largely depend. It may be very difficult, from the nature of their occupation, for some persons, such as those engaged in the liquor traffic, commercial travellers, etc., to become total abstainers. In such instances the advisability of change of occupation or of retiring from business must be considered, and when possible this step should be taken.

Most writers agree that in the last stages of the disease alcohol is necessary; Cheadle,‡ indeed, says that total deprivation of alcohol hastens

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* Roger et Garnier: Rev. de Méd., Feb., 1901, p. 97.

† Bridiers de Villemor: Thèse de Paris, 1893–4, No. 428.

‡ Cheadle: Brit. Med. Journal, 1900, vol. ii, p. 693.

the final collapse. Personally, under such conditions I prefer to give liquor strychninæ in doses of two minims and upwards hypodermically twice a day. The administration of alcohol in the very last stage, when death seems imminent in a few days, is really only a kindly act and directed to inducing euthanasia. Any attempt at curative treatment of the disease is over, and the passing of the bar is made easier, possibly accelerated, by giving alcohol.

Diet.—This is a most important part of the treatment. The object is to minimise autointoxication and to prevent further progress of the cirrhotic process. Milk is the ideal diet. From the fact that the fat in it is well emulsified absorption takes place, even under the difficulties presented by intestinal catarrh and a deficient secretion of bile. The proteid of milk is much less harmful than the proteids of meat, since the putrefactive products derived from it are minimised and the liver is less taxed in the production of urea. Milk has some diuretic action on the kidneys and leaves little residue, so that fermentation and gastro-intestinal autointoxication are much reduced. A patient should be put on milk diet and kept on it till his condition has very markedly improved. Difficulty will often arise in getting the patient to carry out and continue the strict diet, from its monotony.

As much as 3 or 4 pints of milk may be given during the twenty-four hours, or even a larger quantity of skimmed milk. Milk may be diluted with mineral waters, such as soda, Apollinaris, Vichy, Vals, etc. A little bicarbonate of soda may be added with advantage and may do good by antagonizing acid intoxication. Milk may be given as junket, in the form of milk jelly, or flavoured with a little tea, coffee, or cocoa, or as a soup with some vegetable flavouring. Milk should be given every two or two and a half hours during the waking hours. When digestion seems to be defective, milk should be peptonized or given in the form of Benger's food.

In some persons milk gives rise to troublesome nausea. Herter * finds that this can be obviated by reducing the amount of fat in milk, by substituting skimmed milk. The percentage of fat is thus reduced from 4 per cent. to 1 per cent. Koumiss, or fermented mare's milk, may also be given when ordinary milk upsets the stomach, but should not be continued longer than necessary. It is very readily absorbed and may be given in much larger quantities than ordinary milk. Whitla † recommends buttermilk, or the koumiss made in Ireland by mixing half a pint of water, half a pint of buttermilk, and four pints of fresh milk, and one ounce of loaf sugar, leaving in a warm place for thirty-six hours and occasionally shaking.

It has been said, but I do not know with what degree of truth, that a restricted milk diet is well borne by French and Italian, but not by German, patients. A milk diet should be maintained until improvement occurs; eggs and some easily digested farinaceous and proteid foods should be added to the diet, and if these are well borne, pounded fish should be given after an interval. Beef-tea, meat essences, strong soups, and butcher's meat are not advisable. As a change, fruit and vegetables may be occasionally allowed. All stimulating or spicy food should be avoided, such as curries, pickles, anchovies, pickled fish, vinegar, ginger. Fatty food, inasmuch as by fermentation it may give rise to fatty acids, such as acetic, lactic, butyric, valerianic, should be avoided. Coffee and tea should be taken in small quantities freely diluted with milk.

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* Herter, C. A.: Lectures on Chemical Pathology, p. 88.
† Whitla, W.: Dictionary of Treatment, p. 502, 3d ed., 1896.

Carbohydrate Food.—The glycogenic function of the liver is well preserved in spite of the marked histological changes in the organ, and theoretically sugar and starchy foods should be readily assimilated. In practice carbohydrate food should be given in very small quantities and only increased if it is well borne. From the frequency of gastro-intestinal catarrh, fermentation is very likely to take place in sugary food and to give rise to dyspepsia, flatulence, and the production of fatty acids, which when absorbed may further degenerative and cirrhotic changes in the liver.

Drugs.—Iodide of potassium should always be tried in cases thought to be cirrhosis of the liver, on the chance that the condition is in reality syphilitic. Whether iodides do any good in ordinary cirrhosis is very problematical, and no reliance can be placed on this drug or on chloride of ammonium, though it is well to give them a trial. Cases of early cirrhosis often improve under chloride of ammonium, but the other hygienic measures adopted may in reality have been responsible for the good effects ascribed to that drug. Iodoform has been employed internally instead of iodides, but has no advantage over them and may disturb gastric digestion. It is probable that the potash and ammonia given in these drugs are of definite value in counteracting incipient acid intoxication—or acidosis—due to the formation of organic acids of the fatty acid series which tend to diminish the alkalinity of the blood. Whenever the urine gives a port-wine colour with ferric chloride (the fallacy of the reaction with salicylates and other drugs being eliminated), due to the presence of diacetic acid in the urine, bicarbonate of soda should be given in large doses so as to counteract this acid intoxication.

It is very important to prevent or remove gastro-intestinal catarrh, which by leading to the production of toxic bodies aggravates the changes in the liver. This can be most satisfactorily obtained by keeping the bowels freely open by salines, such as sulphate of soda and of magnesia, natural Carlsbad or other mild purgative waters, and by giving fractional doses ($\frac{1}{40}$ to $\frac{1}{20}$ grain) of calomel, which prevent fermentation without purging or interfering with the normal processes of digestion. Arsenic, salicylates, capsicum, and the tinctures and spirituous solutions of drugs should be avoided.

Spa Treatment.—In the very early stages of the disease very considerable benefit may be obtained from a course at some of the numerous spas. The regulated life enjoined when taking the cure and the effects of mildly purgative water in reducing portal engorgement and diminishing intestinal catarrh and fermentation are factors for good in the spa treatment of early cirrhosis, but little real benefit is likely to result in the later stages of the disease, and the fatigue necessitated by the journey is likely to diminish the failing powers of the patient. The following spas may be mentioned: Harrogate, Llandrindod Wells, Vichy, Vals, Ems, Neuenahr, Homburg, Wiesbaden, Baden-Baden, Kissingen, Carlsbad, Marienbad, Franzensbad, Tarasp.

2. PALLIATIVE AND SYMPTOMATIC TREATMENT.

Dyspepsia.—The treatment of dyspepsia must depend on its nature; if it is irritative and due to gastritis, bismuth, dilute hydrocyanic acid, bicarbonate of soda, are indicated. When it is atonic and due to inactivity of the gastric mucous membrane, tonics, such as dilute nitrohydrochloric acid, quassia, liquor strychninæ, should be taken after meals, and pepsin in various forms may be given with food.

For the relief of flatulence intestinal antiseptics, such as creasote, thymol, salol, β-naphthol, salicylate of bismuth, are often recommended, but it is better to give minute doses ($\frac{1}{40}$ to $\frac{1}{20}$ grain) of calomel twice or three times a day or saline purges.

Vomiting from gastritis should be treated by cutting off food for a time and by drugs, such as bismuth, bicarbonate of soda, dilute hydrocyanic acid, or a little morphin. When food is resumed, after a few hours' rest, peptonized milk in small quantities should be given cold. The application of an ice-bag over the stomach has been thought to act as a sedative.

In the earlier stages **constipation** should be prevented by seeing that the patient takes plenty of water, while abdominal massage and gentle exercise may suffice to keep the bowels regular. Mild purgatives and laxatives should be employed if necessary, but powerful drugs, such as elaterium, should be avoided, as they may set up enteritis and exhausting diarrhœa. Salines, such as Epsom or Carlsbad salts; a mixture of two drachms each of sulphate of magnesia and of sulphate of soda; tartrate of soda, or waters, such as Hunyadi János, Friedrichshall, Pullna, Æsculap, Apenta, Franz Josef, may be taken with advantage before breakfast. If these means are not sufficient, a blue pill may be taken overnight in addition, or recourse may be had to small doses ($\frac{1}{6}$–$\frac{1}{2}$ gr.) of calomel, or to cascàra, rhubarb, scammony, euonymin, podophyllin, iridin.

Early in the disease **diarrhœa** or looseness of the bowels may be part of chronic alcoholism; if this is troublesome, bismuth, aromatic chalk and opium mixture, dilute sulphuric acid, tannigen, or, if really necessary, the enema opii, should be given. The diet should, however, be supervised in the first instance, and alcohol strictly tabooed. In the late stage, when toxæmia has developed, diarrhœa may set in and kill the patient. But when slight, it is not always advisable to check the diarrhœa, as it may serve a useful purpose, like diarrhœa in advanced renal disease, in diminishing toxæmia.

Pain over the liver or the minor discomfort of weight and fulness may be relieved by the application of leeches or dry cupping. Relief may be experienced when the liver is enlarged from the application of a bandage to support the organ. Hepatic pain, discomfort, etc., are probably connected with active congestion of the liver, and should be treated by saline purges and by a few 20-grain doses of chloride of ammonium.

The drowsy, semi-comatose condition, due to toxæmia from hepatic insufficiency, may be relieved or even removed by transfusion of saline solution into the muscles or into the veins, the former being the more suitable; the transfusion may be repeated after twenty-four hours. I have seen a patient so improved that he went out of the hospital well: six months later he died of lobar pneumonia; at the autopsy the liver weighed 88 ounces and was markedly cirrhotic. In another case life was prolonged for seven and a half weeks after ascites had disappeared. On the other hand, transfusion sometimes fails or gives rise to very transient improvement. Copious enemata of water may be given, but are not very successful. When diacetic acid is present in the urine, bicarbonate of soda (ʒij to the pint) should be added to the water used for transfusion, so as to counteract auto-intoxication. Hot-air baths often relieve the drowsy, toxæmic condition by making the skin act and so removing poisonous products. Perspiration may be much accelerated by giving a hypodermic injection of pilocarpine (⅛–⅙ gr.) before the bath; the depressing effect of the drug may be prevented by combining it with two minims of liquor strychninæ.

Portal Engorgement.—The chronic venous engorgement of the portal vein which shows itself by enlargement and tenderness, ascites, dyspepsia, and delay in the absorption of food (*vide* opsiuria, p. 230), is treated by saline purges. The increased osmosis into the bowels diminishes the heightened pressure in the portal vein. Sulphate of magnesia and sulphate of soda combined may be given on an empty stomach alone or after a dose of calomel. The good effects are often shown by a considerable diminution in the size of the liver.

Direct puncture of the liver has been occasionally, but usually unintentionally, performed. In a case, mentioned by Goodhart,* where it was done accidentally in performing paracentesis, the woman, who was evidently dying, was greatly improved by the withdrawal of blood from the liver. It is, however, dangerous and should not be countenanced. Abstraction of blood from the spleen by means of a trocar has also been described as giving satisfactory results,† but it is dangerous and cannot be recommended. Massage to the abdomen, and especially to the liver, has been recommended as a means of diminishing the portal congestion (Lecerf ‡) which precedes hæmatemesis.

Administration of Liver Substance.—On the lines of the successful treatment of myxœdema by thyroid extract, attempts have been made to compensate for the disturbance of hepatic function in cirrhosis by giving liver substance by the mouth, or injecting an extract of liver

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* Goodhart: Guy's Hosp. Gaz., May 28, 1898.
† Remlinger: Jour. des Praticiens, Oct. 13, 1901, p. 659.
‡ Lecerf: Thèse Paris, 1901.

(hepatin) under the skin. It has been tried by Vidal,* Gilbert and Carnot,† and others in Paris. Mouras has collected 14 cases of cirrhosis treated in this manner, and though none could be regarded as cured, the results were encouraging; in 7 ascites disappeared and in the others improvement followed. The amounts of urine and of urea were increased, and the quantity of urobilin in the urine was diminished. The liver of the pig is employed; as much as 3½ ounces of pulped liver were given daily by Vidal with successful results. The only bad effect appears to be diarrhœa.

3. TO PROMOTE THE COMPENSATORY MECHANISMS BY MEANS OF WHICH THE DISEASE BECOMES LATENT.

Since no drug has the power of producing absorption of the fibrous tissue, any attempts to cure the disease must be directed to improving the compensatory mechanisms which enable the disease to become latent. Nature's compensatory efforts in cirrhosis are (*a*) increase in the collateral circulation between the branches of the portal vein and the general systemic veins (*vide* p. 209) and (*b*) hyperplasia of the liver cells. These compensatory mechanisms have already been discussed in the section on Prognosis, and the operation of promoting vascular adhesions around the liver was described in the section on the Treatment of Ascites.

Hyperplasia of the Liver Cells.—There is no drug, as far as is known, that can safely be employed for this purpose, though one would naturally turn to arsenic as likely, from its power of stimulating growth elsewhere, to have this effect. Whether it has this effect on the liver there are, as far as I know, no experiments to show. A drawback to its use in patients with cirrhosis is that if given by the mouth it might set up gastro-intestinal irritation and autointoxication in the alimentary canal; and, indeed, there is reason to believe, both from increased frequency of ascites during the epidemic of arsenical poisoning in the north of England in 1899–1900 and from experimental results, that arsenic may set up cirrhosis. In the present state of our knowledge the administration of arsenic in cirrhosis is contraindicated. As was pointed out elsewhere, it is theoretically possible that the surgical production of vascular adhesions around the liver may so improve the circulatory conditions as to favour hyperplasia of the hepatic cells. It is hardly necessary to add that the general health should be improved as far as possible and that fresh air, sun, and careful feeding are important factors in the treatment.

PIGMENTED CIRRHOSIS.

In the description of the histological appearances of portal cirrhosis it was pointed out that pigmentation of the liver cells and of the fibrous tissue may occur under certain conditions and that some slight pigmentation of the cells is not uncommon, if carefully sought for, in ordinary examples of that disease. Pigmentation of a cirrhotic liver may, in exceptional instances, be due to foreign particles of carbon, stone, or metals reaching it by the blood-stream (*vide* Cirrhosis anthracotica). Some degree of pigmentation with hæmosiderin, an iron-containing derivative of hæmoglobin, may be seen in cirrhotic livers after local hæmorrhages into the substance of the organ.

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* Vidal: Soc. de biolog. Paris, Nov. 28, 1897.

† Gilbert and Carnot: Soc. de biolog. Paris, Nov. 21, 1897.

In the foregoing instances the amount of pigmentation is comparatively small and of little importance. The more important forms of pigmented cirrhosis are (i) that occurring in hæmochromatosis and bronzed diabetes, and (ii) malarial pigmentation of a cirrhotic liver.

CIRRHOSIS ANTHRACOTICA.

This is a very rare condition in which cirrhosis of the liver is associated with the presence of small masses of carbon in the organ. It is analogous to anthracosis of the lungs (coal-miner's lung). Welch * has described such a case and Adami † speaks of a similar condition in relation to silicosis. The condition is probably not so rare as the paucity of recorded cases would suggest, and as it may not be detected unless the liver is microscopically examined, cases are probably not infrequently overlooked. The following case was examined by me in 1892.

A chimney-sweep aged forty-seven was admitted to St. George's Hospital on June 4, 1892, with a transverse fracture of the left leg; a month later he had parotitis, and on September 8 he became jaundiced and ascitic; ten days later the abdomen was tapped, and on September 25 he died from asthenia. The trachea, lungs, and stomach were deeply pigmented. The liver (59 ounces) was cirrhotic, but not pigmented to the naked eye. Microscopically there was old multilobular cirrhosis with rather extensive pigmentation of the fibrous tissues. The pigment was black and amorphous, quite different from the yellow pigment of hæmochromatosis, and was probably soot conveyed by the portal vein to the liver. Its presence was discovered only as the result of microscopic examination, and it is quite possible that such pigmentation of sweeps' livers in some degree is not uncommon.

PIGMENTARY CIRRHOSIS OF HAEMOCHROMATOSIS.

Synonym: Diabète Bronzé.‡

History and Etiology.—The condition of bronzed diabetes, or diabète bronzé, was first noticed by Troisier in 1871, and was referred to by Trousseau in his clinical lectures. Hanot and Chauffard in 1882 described two cases of diabetes with enlarged and pigmented cirrhotic livers. In 1886 Hanot, in collaboration with Schachmann, described a further case and defined the condition as a definite morbid entity under the name "diabète bronzé." They took the view that the diabetes was the primary lesion, and that as a result the hepatic cell became stimulated to an increased production of pigment. Further cases of diabète bronzé were described by the French school: Letulle (1885), Brault and Galliard, Barth, Mossé, Marie, Auscher and Lapique, Meunier, Rabé, and others.

Letulle believed that as a result of hyperglycæmia the pigment was formed from the hæmoglobin by the cells of various organs, and that it was stored up in the liver cells, though not produced there. In France, where most of the cases have been described, the association with diabetes has been insisted on, and only five cases of this variety of cirrhosis without glycosuria have been reported by French observers. In Germany more attention has been paid to general pathological pigmentation without glycosuria. In 1889 v. Recklinghausen described the condition of hæmochromatosis, which consists in infiltration of the organs with pigment derived from pathological destruction of the red blood-corpuscles.

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* Welch, W. H.: Johns Hopkins Hosp. Bull., 1891.

† Adami, J. G.: Sajous' Annual, 1898, article "Cirrhosis."

‡ The bibliographical references will be found on p. 304.

It has been suggested by Opie that there is a toxic material which both causes hæmolysis and acts on the cells of the liver and other organs so that they transform into insoluble hæmosiderin the soluble blood pigment reaching them. Meunier, indeed, by repeated injections of toluylendiamine into dogs, produced pigmentation of the liver and other organs with an iron-containing body, but did not obtain results on the same dimensions as in hæmochromatosis. Adami and M. Abbott regard bacterial activity as the cause both of the hæmolysis and of the degenerative changes in the cells of the pigmented viscera, and bring forward facts to suggest that it is a chronic intestinal infection. Adami compares it with pernicious anæmia and describes the pigment as forming in and around the dead diplococcal forms of the colon bacillus.

The *pigmentation* occurs, as was shown by the French observers, in the cells of the liver, pancreas, secreting glands, in the interstitial tissue of these organs, in the lymphatic glands, and in the heart-muscle, intestines, and skin. In the muscular fibres of the intestines and heart a yellow, iron-free pigment called hæmofuscin is found. The relation of these two pigments offers scope for discussion, and though it seems probable that the same conditions may lead to their formation, they are independent. Goebel has found this iron-free pigment in the smooth muscular fibres of various organs in persons of advanced years, so that it may be regarded as being more or less physiological, though in hæmochromatosis it is present in large quantities.

The pigmentation of the skin is due to an iron-free pigment, apparently the same as the normal one. (Opie.) The muscular fibres of the heart contain both hæmosiderin and hæmofuscin. In the earlier stages of hæmochromatosis the pigment accumulates in the cells of the organs, the liver being the most markedly affected. As the cells become infiltrated with pigment, they progressively degenerate, undergo necrosis, and liberate the pigment, which passes into the interstitial fibrous tissue of the organ. Interstitial fibrosis of the liver and pancreas develops in the wake of the pigmentary change. When the fibrosis of the pancreas reaches such a degree that the islands of Langerhans are involved, diabetes results. The production of diabetes mellitus is therefore a late result of the hæmochromatosis. (Anschütz.) Of five cases described in America (Osler, Opie, Maude Abbott, Condon), there was diabetes in one only (Condon's case). Only three cases have been described in England, those by Saundby, Galloway, and G. Parker, but the condition is not nearly so rare as this.

A man aged fifty-two died in a drowsy state after paracentesis for ascites in 1902 under my care in St. George's Hospital. The liver was cirrhotic and of a greenish-blue colour, but did not arouse any suspicion of hæmochromatosis until it was microscopically examined. Multilobular cirrhosis with very well-marked hæmochromatosis was then found. During life there had been no glycosuria, and the skin, though somewhat earthy in colour, was not noticeably pigmented. The pancreas was not kept for microscopic examination, as the body was decomposed and no suspicion of hæmochromatosis arose until after microscopic examination of the liver. I have seen extensive hæmochromatosis with slight cirrhosis in a liver showing secondary endotheliomatous growths. There is a piece of a liver showing a simple cyst in the museum of St. Bartholomew's Hospital which has the characteristic brick-red colour of the liver in hæmochromatosis.

Probably cases of pigmentation of the liver found after death and often assumed to be due to past malaria are in reality examples of hæmochromatosis.

Age.—The condition of hæmochromatosis occurs chiefly between forty and fifty years of age.

Sex.—In 30 cases mentioned by Letulle * the male sex only was affected. M. Abbott's case is the only one in which a woman was the subject of the disease.

Morbid Anatomy.—The liver is nearly always enlarged, sometimes considerably; the left lobe may be more enlarged than the right. The organ has a striking deep-red or maroon colour, resembling that of brick dust or iron rust, and shows multilobular cirrhosis. As might naturally be expected, the pigmented liver is less permeable to Röntgen rays than a normal one. (Jeanselme.) Microscopically there is brownish-yellow pigment, which gives the reaction for iron with ferrocyanide of potassium and hydrochloric acid (Perl's test); it is present in the liver cells, in the endothelial cells lining the vessels, in Kupffer's star-like connective-tissue cells, and in the fibrous tissue between the enclosed lobules. The pigment collects first in the liver cells in the periphery of the lobules; as it accumulates the cell nucleus shows signs of degeneration, and eventually the cells necrose and break up. The pigment is then carried along the lymphatics into the fibrous tissue of the cirrhotic liver and there forms large masses. There is ordinary multilobular cirrhosis. The hepatic artery shows endarteritis obliterans. In the muscular coat and adventitia of the arteries and veins a pale-yellow pigment, which contains no iron and is called hæmofuscin, is seen. It remains unchanged when exposed to ferrocyanide of potassium and hydrochloric acid.

The *spleen* is enlarged, firm, and pigmented. The *pancreas* is enlarged and pigmented, and shows chronic interstitial fibrosis. The *intestines* are pigmented from hæmofuscin in the muscular fibres and hæmosiderin in the epithelial cells of the glands.

The symptoms may be those of cirrhosis or of diabetes. In the latter event the condition is spoken of as bronzed diabetes (diabète bronzé). The signs are generalized pigmentation with enlargement of the liver and spleen. The pigmentation of the skin imitates that of Addison's disease; it may be of a slaty colour and might suggest the rare condition of argyria, where the skin becomes permanently discoloured as the result of the medicinal use of silver salts. Generalized pigmentation is present in most but not in all the cases; where it is absent the existence of pigmented cirrhosis is, of course, only discovered after death.

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* Letulle: Soc. Méd. des Hôp., 1897.

The enlargement of the liver and spleen may be considerable. The liver is usually, but not always, bigger than in health. The enlargement of the liver and spleen is usually progressive and relatively equal. (Osler.*) In a certain number of cases hæmorrhages may occur, and in a few instances there have been recurrent attacks of purpura. Abbott's case died of hæmorrhage from an ulcerated œsophageal varix. In most cases there is little or no ascites and the subcutaneous abdominal veins may be dilated. There may be dyspepsia and pain on the right side of the abdomen. Diabetes is a late phenomenon and does not always supervene; when it does, it usually appears a year before death. The onset may be somewhat abrupt, with weakness, diarrhœa, œdema of the legs, and lead to death from coma or from destructive lung changes.

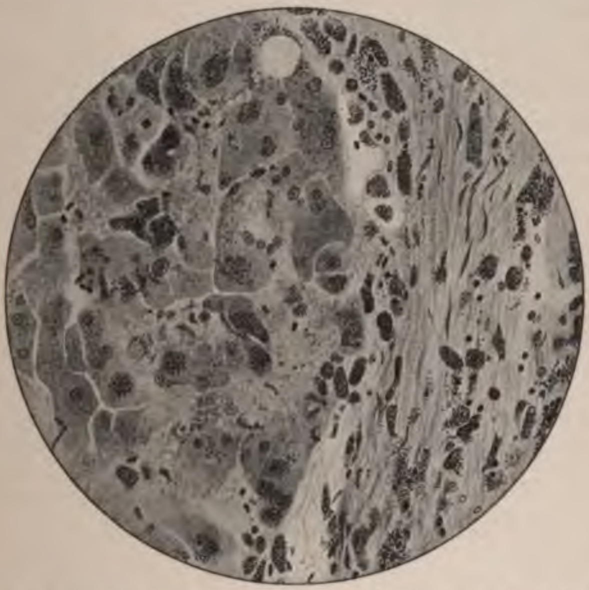

FIG. 36.—SHOWS PIGMENTATION OF THE LIVER CELLS AND FIBROUS TISSUE IN CIRRHOSIS OF HÆMOCHROMATOSIS.

Some of the pigmented cells show signs of degeneration, and in some instances the outlines of the cells around the collections of pigment have gone. (From case described by Dr. Maude Abbott, of Montreal, who kindly provided me with some of the liver.) × 220.

Diagnosis.—Signs of cirrhosis with glycosuria and pigmentation of the skin are the three factors which justify a certain diagnosis of the condition. In cases of cirrhosis with marked cutaneous pigmentation, but with no glycosuria, the disease may be suspected, but usually cannot be positively diagnosed, since considerable pigmentation, especially of a dirty earthy colour, may exist in ordinary cirrhosis, while the effects of past jaundice may discolour the skin.

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* Osler: American Journ. Med. Sciences, vol. cxxiv, p. 766 Nov., 1902.

Differential Diagnosis.—From *Addison's* disease the enlargement of the liver and spleen and glycosuria should distinguish it. In some instances of *hypertrophic biliary cirrhosis* the colour of the skin may resemble that of hæmochromatosis, but the existence of jaundice as shown by the conjunctivæ should prevent a mistake. In *chronic splenic anæmia* there is sometimes cutaneous pigmentation, possibly from the effects of arsenic given medicinally, and some resemblance to hæmochromatosis without glycosuria might occur. The spleen is greatly enlarged in splenic anæmia, and only moderately in hæmochromatosis, while the course of the disease is usually prolonged in splenic anæmia.

In most exceptional cases alcaptonuria may be associated with remarkable pigmentation of the face, ears, and internally of the costal cartilages (*ochronosis*, Virchow). In these cases the reduction of copper by the urine might suggest bronzed diabetes; further examination of the urine would, however, show that there is no sugar present.*

Prognosis is bad. Life may be prolonged for years and death may occur from gastro-intestinal hæmorrhage as in cirrhosis. When diabetes appears, the fatal termination is usually not delayed beyond a year.

Treatment.—If there is diabetes, the treatment should be directed to that condition by appropriate dieting, codeia, etc. Since the diabetes is undoubtedly pancreatic in origin, it would be reasonable to try the administration of extract of pancreas, but so far the results are not encouraging. Before the development of glycosuria the treatment should be the same as that of early cirrhosis, viz., a bland diet and drugs directed to prevent intestinal fermentation and putrefaction.

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* For information on this subject I am indebted to Professor W. Osler and Dr. Garrod. H. Albrecht's paper (Zeitschrift f. Heilkunde, Bd. xxiii, S. 366, 1902) should be referred to.

Osler: Brit. Med. Journ., 1899, vol. ii, p. 1595. Lancet, 1904, vol. i, p. 10. (Ochronosis).
Futcher: Journ. American Med. Assoc., Sept. 28, 1901, p. 815.
Condon: American Medicine, Dec., 1900.
Saundby: Lectures on renal and urinary diseases, p. 321, 4th ed., 1900.
Galloway: Brit. Journ. of Dermat., vol. ix, p. 32, 1897.
Parker, G.: Brit. Med. Journ., 1903, vol. ii, p. 1052.
Rendu and de Massary: La Presse Médicale, Feb. 6, 1897.

MALARIAL PIGMENTATION OF A CIRRHOTIC LIVER.

In the past malaria was regarded as an established cause of hepatic cirrhosis, and several forms of malarial cirrhosis were described. Frerichs, Lancereaux, and Kelsch and Kiener * recognised malaria as a cause of hepatitis. Kelsch and Kiener have described in great detail the changes induced in the liver by chronic malaria. In one form, called "hyperæmia phlegmasique," the liver is large, shows perihepatitis, cloudy swelling of the liver cells, and small-cell infiltration of the portal spaces. In another form, nodular parenchymatous hepatitis, the liver is larger and soft and shows numbers of small nodules composed of liver cells undergoing hyperplasia. Cirrhosis may subsequently develop. Kelsch and Kiener believed that the fibrosis was due to a process of metaplasia on the part of the liver cells, but the view that connective tissue is formed from epithelial cells is entirely opposed to modern pathological teaching. The resulting cirrhosis is described as either monolobular or multilobular. Both the fibrous tissue and the liver cells are infiltrated with pigment.

Osler,† on the other hand, says that during nine years' practice at the Johns Hopkins Hospital there was not a single case of advanced cirrhosis due to malaria. Welch is quoted by Barker ‡ as having seen only one case of malarial cirrhosis in New York, and that in an Algerian. Hale White § regards malarial cirrhosis as largely imaginative.

As Barker points out, the degenerative and necrotic changes in the liver cells produced by severe malarial infection are exactly the conditions favourable to the production of chronic interstitial fibrosis of the liver. Further, in malaria there may be considerable gastro-intestinal disturbance which might lead to cirrhosis of the liver, and it has also been thought that the production of poisons in the spleen might lead to secondary cirrhosis. (Chauffard,‖ *vide* p. 189.) Barker has suggested that the pigmentation of the liver cells, which is most marked in the peripheral parts of the lobules, may act as an irritant and set up fibrosis of the organ, in the same way that the inhalation of carbon particles induces chronic interstitial pneumonia.

Without denying the possibility that the necrotic changes in the liver cells induced by malaria may be succeeded by cirrhosis, this sequence of counts is evidently so rare that when cirrhosis occurs in a malarial subject the question must arise whether it is cirrhosis caused by malaria or merely cirrhosis in a malarial patient. Alcohol and intestinal toxæmia may be potent causes of hepatic cirrhosis in patients suffering from chronic malaria, or a patient with latent cirrhosis may be attacked with malaria. In either of these events the liberated blood pigment may be deposited in the liver and produce a pigmented cirrhosis. Clinically there is nothing very special in the signs of cirrhosis in a malarial subject. The signs are those of ordinary portal cirrhosis terminating with ascites. The spleen is enlarged, and from the influence of malaria more markedly so than in ordinary portal cirrhosis.

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* Kelsch and Kiener: Archiv de Physiol. norm. et path., 1878, p. 571; 1879, p. 354.

† Osler, W.: Practice of Med., 4th ed., 1901, p. 570.

‡ Barker: Johns Hopkins Hospital Reports, vol. v, p. 241.

§ Hale White: Brit. Med. Journ., 1903, vol. i, p. 533.

‖ Chauffard: La Sem. méd., p. 177, 1899.

BILIARY CIRRHOSIS.

Biliary cirrhosis will be considered under two distinct heads: (i) Hypertrophic biliary cirrhosis, and (ii) obstructive biliary cirrhosis.

HYPERTROPHIC BILIARY CIRRHOSIS.

It is sometimes spoken of as "hypertrophic cirrhosis." This is likely to lead to confusion, as there are several other kinds of large cirrhotic livers; in common or portal cirrhosis the organ is often much enlarged, a fatty cirrhotic liver is of very considerable size, and the pigmented cirrhotic liver in hæmochromatosis is also entitled to the adjective hypertrophic. The term "hypertrophic cirrhosis" should therefore be given up.

Definition.—The disease is characterized by chronic jaundice, periodic febrile attacks, absence of ascites, enlargement of the liver and spleen, and by its preference for young persons. There is no gross obstruction to the larger bile-ducts, and histologically the cirrhosis is more monolobular than in portal cirrhosis.

HISTORY.

Although the condition was recognised by Requin * in 1846, by Todd † eleven years later (1857), and by Hayem ‡ in 1874, it attracted little attention until Hanot § (1876) sharply struck out the disease in his thesis on "Hypertrophic Cirrhosis with Chronic Jaundice."

Hanot's thesis was based on fifteen cases, four of which he had observed during life; in three of the four a postmortem examination was obtained.

In 1893 Kiener ‖ suggested that the disease should be called Hanot's disease. Since then somewhat different though allied forms of hypertrophic biliary cirrhosis have been described in France (*vide* p. 307), and discussion has arisen as to the channel by which the cause of the disease reaches the liver. Of late years the opinion has been growing that the description given by Hanot was too sharply crystallised, and that few cases conform to the rigid type he erected. It has also been suggested that the symptoms and signs do not correspond to any one type of anatomical change in the liver, but may be associated with various forms of cirrhosis. The prevalent view in this country, as voiced by Hawkins * and Pye Smith,† is that no real distinction can be drawn between portal and hypertrophic biliary cirrhosis. This depends on the fact that the clinical features of hypertrophic biliary cirrhosis undoubtedly occur in cases which on minute pathological examination show the changes of portal cirrhosis. This discrepancy between the clinical picture and the pathological changes is probably due to the fact that cirrhosis, wherever it begins, will after a time spread and lead to changes of the nature of a mixed cirrhosis. Thus there is a special tendency for changes presumably beginning in the small bile-ducts to become complicated in course of time by those of portal cirrhosis. After much consideration of the question I have come to the conclusion that there is an essential difference, both clinically and pathologically, between portal and hypertrophic biliary cirrhosis, and that Hanot and the French school are fully justified in their contention. No doubt transitional forms between the two types of cirrhosis occur, just as they do between the arteriosclerotic (granular) kidney and that of chronic parenchymatous nephritis (large white kidney); but it would be incorrect to assume that they are different manifestations of one and the same process. Although different types exist, it is advisable to give an inclusive description of the disease as a whole, and to draw attention to the varieties which may occur.

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* Requin: Pathologie Médicale, tome ii, p. 748.
† Todd: Med. Times and Gaz., Dec. 5, 1857, p 571.
‡ Hayem: Archiv de Physiol. normal et path., 1874.
§ Hanot: Thèse Paris, 1876.
‖ Kiener: La Sem. Méd., July 19, 1893.

DIFFERENT FORMS OF HYPERTROPHIC BILIARY CIRRHOSIS.

A number of cumbrous names have been coined to distinguish varieties of the disease. These varieties depend on differences in the degree of the splenic and hepatic enlargement, and on the relationship between the enlargement of the two organs, both in size and in the data of appearance. These types, created by Gilbert and by Chauffard, will be referred to again in the description of the physical signs of the disease, but it may be well to give a list of them here.

Ordinary form of hypertrophic biliary cirrhosis, described by Hanot, in which the liver and spleen are both enlarged.

Splenomegalic form, in which the splenic enlargement is the predominant feature.

Hypersplenomegalic form, in which the spleen is actually larger than the liver.

Metasplenomegalic form, in which splenic enlargement precedes any manifest change in the liver.

Hepatomegalic or asplenomegalic form, in which the enlargement of the liver is the prominent feature.

Presplenomegalic form, in which the enlargement of the liver precedes that of the spleen.

Atrophic biliary cirrhosis, in which the liver is small.

A special juvenile type with great splenic enlargement was described by Gilbert and Fournier,[*] and a remarkable form of biliary cirrhosis has been described by Gibbons and others in native infants in Calcutta. (*Vide* p. 187.)

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* Hawkins: Allbutt's System of Medicine, vol. iv, p. 185.

† Hilton Fagge and Pye Smith: Practice of Medicine, vol. ii, p. 540, 1902.

In the cases in which the spleen is considerably enlarged before the liver is noticed to be affected—metasplenomegalic hypertrophic biliary cirrhosis—Chauffard [†] believes the hepatic cirrhosis to be due to poisons manufactured in the spleen, and that the disease is a different one from the ordinary type. There is a gradual transition from the less marked examples of metasplenomegalic biliary cirrhosis to Banti's disease or splenic anæmia with a terminal cirrhosis. Cases without jaundice, "Cirrhoses biliaires anicteriques," have also been described.

On Some Forms of Disease Possibly Allied to Hypertrophic Biliary Cirrhosis.—As in many other diseases, there are less characteristic cases ("fruste" or larval) which present some of the features of biliary cirrhosis, but are incomplete and wanting in others. Thus, as just mentioned, there may be transitional cases between splenic anæmia and hypertrophic biliary cirrhosis.

Thus Claude Wilson [‡] described a family in which six individuals in three generations had anæmia, enlarged spleens, and periodic attacks of jaundice and abdominal pains. In one of these cases a postmortem examination showed that the liver was free from cirrhosis. These cases were, therefore, more allied to splenic anæmia than to biliary cirrhosis, though clinically the resemblance to metasplenomegalic biliary cirrhosis must have been considerable. Sir T. Barlow and H. B. Shaw[§] have published two cases of recurrent attacks of jaundice and of abdominal crises with hepatosplenomegaly, occurring in a mother and son, which seem to form a kind of connecting link between hypertrophic biliary cirrhosis and chronic splenic anæmia. Hayem [‖] in 1898 described the clinical aspect of a condition which he regarded as a chronic form of Weil's disease, and called chronic infectious jaundice with splenic enlargement and exacerbations. As none of his five cases was examined after death, it is impossible to say with any exactitude what was the nature of the condition; but it is probable that these cases and those of Barlow and Shaw are closely allied. Lereboullet [**] includes Hayem's cases together with 5 of his own, 3 of Boinet's,[††] and one of Bettmann's,[‡‡] and Minkowski's [§§] in a group under the name of chronic splenomegalic jaundice. Minkowski's case was examined after death and the liver was found to be free from cirrhosis. The title is convenient in being non-committal.

Incidence.—Genuine cases of hypertrophic biliary cirrhosis are distinctly rare; this contrasts with the frequency with which common or portal cirrhosis is met with. The rarity of the disease is perhaps not fully recognised since cases of ordinary cirrhosis with large livers but without chronic jaundice are not infrequently confused with it.

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[*] Gilbert and Fournier: Soc. de biolog., March 26, 1898.

[†] Chauffard: Semaine Médicale, 1900, p. 176.

[‡] Claude Wilson: Trans. Clin. Soc., vol. xxiii, p. 162, and (with D. Stanley) vol. xxvi, p. 163.

[§] Barlow and Shaw: Trans. Clin. Soc., vol. xxxv, p. 155.

[‖] Hayem: La Presse Médicale, March 9, 1898.

[**] Lereboullet: Paris Thèse, No. 180, 1902, Les Cirrhoses biliaires.

[††] Boinet: Archiv. Général. de Méd., 1898.

[‡‡] Bettmann: München. med. Wochen., June 5, 1900, S. 791.

[§§] Minkowski: Verhandlungen Congres. f. inn. Med., Wiesbaden, 1900.

ETIOLOGY.

Age.—It is commonest between the ages of twenty and thirty and is rare after forty, thus again contrasting with common cirrhosis, in which the average age is about forty-eight years. A considerable number of cases are met with in young children (Gilbert and Fournier's juvenile type).

Sex.—In children the incidence of the disease falls equally on the two sexes, but apart from these juvenile cases it appears that males are more often attacked. In Schachmann's[*] 26 cases only 4 were females.

Heredity.—The disease is sometimes met with in several members of the same family when exposed to the same conditions.

Finlayson[†] described three cases in one family. Dreschfeld[‡] recorded the disease in two brothers, and Osler[§] had a similar experience in America. Boix,[‖] Boinet,[**] and Hasenclever[††] have also published similar groups of cases. In Brahmin infants in India a form of cirrhosis described as biliary is very common, and is especially apt to attack members of the same family; thus, as many as fourteen children of the same parents have died of it, one after another. But it is by no means certain that these cases are the same as Hanot's disease. Scheube,[‡‡] in fact, regards them as parasites and possibly due to distoma in the bile-ducts, but this also seems unlikely. The condition is referred to elsewhere (p. 187).

The disease may be found in more than one generation, as shown by Boix and Boinet, but probably this depends on the surroundings more than on direct heredity. It is interesting to note that in other members of the same family who have no symptoms of disease the spleen may be found to be enlarged (Boix, Boinet); this is analogous to the loss of knee-jerk in apparently healthy members of a family containing some children affected with hereditary ataxia.

In one family the father and two children had fully developed hypertrophic biliary cirrhosis, while three other children had big spleens. (Boinet.)

Lereboullet[§§] has described the "cholemic family," the members of which are supposed to be specially susceptible to infection of the bile-ducts, much in the same way as other families are rheumatic or tuberculous. Patients with this diathesis are probably more likely to become the subjects of hypertrophic biliary cirrhosis than ordinary persons.

Alcoholism.—The antecedents of patients with hypertrophic biliary cirrhosis sometimes include heavy drinking, but there is no reason to regard alcoholism as related to the disease in the same way as it is to common cirrhosis. It may safely be said that alcoholic excess does not protect against biliary cirrhosis, but, on the contrary, that it may dispose to infection by reducing the resisting power of the body as a whole and of the liver in particular. Of the two brothers whose cases were recorded by Dreschfeld, one was a hard drinker while the other was temperate. Boix has recently put forward the view that the infection is introduced into the body in water, and it has been thought that cold and damp houses favour the occurrence of the disease.

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[*] Schachmann: Thèse Paris, 1887.

[†] Finlayson: Glasgow Hospital Reports, vol. ii, p. 39, 1899.

[‡] Dreschfeld, J.: Medical Chronicle, April, 1896.

[§] Osler: Practice of Medicine, p. 574, 4th edition.

[‖] Boix: La Presse Médicale, March 16, 1898.

[**] Boinet: Archiv. Général. de Méd., April, 1898, and 1903, p. 362.

[††] Hasenclever: Berlin. klin. Wochen., Nov. 7, 1898.

[‡‡] Scheube: The Diseases of Warm Climates, p. 364.

[§§] Lereboullet: Les Cirrhoses biliaires, Thèse Paris, No. 180, 1902.

Malaria, etc.—In some instances malarial infection has preceded the development of the disease, but in the majority of instances this can be ruled out of court.

Géraudel * has revived Lancereaux's view of 1871—that the signs and symptoms ascribed to the disease are malarial in origin.

There is no reason to believe that syphilis or tuberculosis plays any special part in the causation of the disease. It has been noticed to develop after typhoid fever in a few isolated cases. (Boinet.)

Infective Origin.—Hanot originally regarded the initial lesion as a catarrhal inflammation of the small bile-ducts. Such a lesion might originate in the minute ducts and be due to a poison reaching them by the blood, as in experimental poisoning by toluylendiamine; in other words, a descending cholangitis. The condition of the liver would then be a local manifestation of a general toxæmic or infective process. In favour of an infective origin for hypertrophic biliary cirrhosis the following points may be urged:

1. The frequency of fever.
2. The considerable splenic enlargement, which indeed may precede or be more marked than that of the liver.
3. Glandular enlargement, not only in the portal fissure, but occasionally in more distant parts of the body.

The enlargement of the spleen, which may precede and be more prominent than the hepatic enlargement, may be explained as due to an infective agent in the blood, which at the same time as it leads to changes in the liver, settles down in the spleen and there multiplies and produces toxic bodies. It is not improbable that the poison thus manufactured passes into the portal vein and sets up a secondary portal cirrhosis (*vide* Cirrhosis of Splenic Origin, p. 189) on the top of the already existing biliary cirrhosis, and thus accounts for the confused and mixed type of cirrhosis so often found in the livers of long-standing cases of biliary cirrhosis. In cases where the spleen becomes manifestly enlarged before the liver (metasplenomegalic form of biliary cirrhosis) is affected, the liver is probably more resistant to infective or toxic influences than in the ordinary cases of biliary cirrhosis.

The alternative view is that hypertrophic biliary cirrhosis is due to a local infection of the bile-ducts from the duodenum—an ascending cholangitis. According to this theory, it would be analogous to bronchopneumonia following bronchitis of the larger tubes. Gilbert and Fournier † regard it as an ascending infection from the intestine and due to the prolonged action of bacilli belonging to the colon group. Potain ‡ and other French observers held the same view. The enlargement of the spleen is regarded as secondary to the local and primary infection of the liver and due to micro-organisms or their poisons absorbed from the infected bile-ducts. In favour of this view is the fact that in some cases, which have been operated upon during life and the gall-bladder drained, micro-organisms such as the Bacillus coli and Diplococcus pneumoniæ have been found in the biliary tract. The operative treatment of hypertrophic biliary cirrhosis is referred to below (*vide* p. 326); there may be some question whether all the cases included in Greenough's * list of seventeen operations were genuine examples of hypertrophic biliary cirrhosis, but the marked success in 13 of the cases must be regarded as weighty evidence in favour of an ascending infection.

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* Géraudel: Thèse Paris, 1902.
† Gilbert and Fournier: Soc. de biolog., July 10, 1897.
‡ Potain: Semaine Médical, 1896, p. 101.

Against the view that it is an ascending infection might be urged the comparative infrequency of dyspepsia as an antecedent symptom and the fact that a catarrhal condition of the duodenum is not found at the autopsy. The fact that the spleen may be enlarged before the liver, and before there is any jaundice which may be regarded as evidence of infection of the bile-ducts, is against the theory of an ascending infection and in favour of the primary factor being a general hæmic infection. If the condition were due to an ascending infection from the duodenum, the pancreatic duct should also become infected, and as a result chronic interstitial pancreatitis with increase in the size of the head of the pancreas should occur.

Guillain † has described such a condition, under the name of "Sclérose hépato-pancréatique hypertrophique avec hypersplénomégalie," in a temperate woman aged fifty-two years; there were hypertrophic biliary cirrhosis and enlargement of the pancreas to double its normal size. He regarded the condition as due to an ascending infection.

In biliary cirrhosis, however, the pancreas is not enlarged, as is shown by Lefas' ‡ statistical observations, so no support to the theory that biliary cirrhosis is due to an ascending infection is forthcoming on these grounds. On the whole, it seems more probable that hypertrophic biliary cirrhosis is due to a hæmic infection of a chronic nature leading to inflammatory changes in the liver, than that it is an ascending infection of the bile-ducts from the duodenum.

Congenital obliteration of the bile-ducts which is associated with a mixed (multilobular and monolobular) cirrhosis of the liver, can be regarded as in part due to a poison circulating in the blood, which when excreted into the small bile-ducts sets up a descending cholangitis. This cholangitis leads to union of the inflamed surfaces of the larger ducts, analogous to obliteration of the vermiform appendix after catarrhal appendicitis.

Possibly among the different forms of hypertrophic biliary cirrhosis there are some cases, like Guillain's type, due to an ascending infection, though the majority are, like scarlatinal nephritis, due to a poison reaching the liver by the general circulation. A question which cannot at present be answered is whether poisons reaching the liver by the portal vein ever set up the lesions of hypertrophic biliary cirrhosis. As shown by experiments with toluylendiamine, poisons in the general circulation are excreted into the small bile-ducts and set up inflammation of the smaller ducts; this is analogous to hypertrophic biliary cirrhosis. As far as we know, poisons arriving by the portal vein tend to produce common (portal) cirrhosis. An exception, however, must be made for congenital syphilis, where the fibrosis is intercellular.

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* Greenough: American Journ. of Med. Sciences, vol. cxxiv, p. 979.
† Guillain: Rev. de Méd., Sept., 1900, p. 701.
‡ Lefas: Archives Générales de Médecine, May, 1900, p. 539

Bacterial Origin.—Although a specific origin for the disease has been anticipated, no microbic cause has yet been satisfactorily established. The colon bacillus has been found in blood withdrawn by puncture from the liver during life and subsequently in the liver and spleen in the same case (Gilbert and Fournier[*]). But further evidence must be brought forward before the colon bacillus can be regarded as the specific cause. Hayem,[†] in his cases of chronic infective jaundice with splenic enlargement and exacerbations, which is very closely allied to, if not the same disease as, hypertrophic biliary cirrhosis, found the Diplococcus pneumoniæ in blood aspirated from the spleen during life. A diplococcus has also been described by Kirckow[‡] as the cause of the disease.

MORBID ANATOMY.

The liver is uniformly enlarged and usually weighs from 80 ounces upwards; it may reach a weight of eight pounds or even more.

In very exceptional cases the liver is described as smaller than natural—"atrophic biliary cirrhosis." It does not seem clear that Weber's[§] case, sometimes quoted as an example of atrophic biliary cirrhosis, in which the liver of a girl aged fourteen years was hobnailed and weighed 26½ ounces, was not one of ordinary portal cirrhosis.

Perihepatitic adhesions uniting the liver to the diaphragm are not uncommon, but otherwise the surface is fairly smooth, and is at most finely granular. It does not present the gnarled and hobnailed appearance of common cirrhosis. In long-standing cases secondary portal (multilobular) cirrhosis supervenes and the surface may be irregular. It is of a dark-green colour and on section is firmer than natural and has an aspect like granite, due to the fine mesh of the fibrosis.

The portal vein and the hepatic artery show no signs of inflammation. The gall-bladder contains bile and is usually healthy, though its walls are sometimes thickened. The larger bile-ducts appear normal. It is remarkable, inasmuch as there is cholangitis, that bilirubin-calcium calculi are not more often present in the ducts. Gall-stones have been found in cases of hypertrophic biliary cirrhosis, and can be quite well explained as a secondary formation; it it not necessary to assume that they are primary and the cause of the cirrhosis.

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[*] Gilbert and Fournier: Compt. Rend. Soc. de biolog., July 10, 1897.

[†] Hayem: La Presse Médicale, March 9, 1898.

[‡] Kirckow: Bolnichnaja Gazeta Botkina, 1900. Quoted in Rev. de Méd., July, 1901, p. 727.

[§] Weber, F. P.: Trans. Path. Soc., vol. xlvi, p. 71, 1896.

Microscopic Appearances.—The liver shows fibrosis, which in the earlier stages is monolobular and tends to surround each lobule, much in the same way, though not so diagrammatically, as in a normal pig's liver. In looking at a section in the early stages the monolobular arrangement is well seen and forms a contrast to multilobular cirrhosis. But in long-standing cases the fibrosis is often irregular and there is usually multilobular cirrhosis as well. This is confusing, and no doubt accounts for the difficulty experienced by many writers in accepting hypertrophic biliary cirrhosis as a distinct pathological type. This multilobular cirrhosis is, I believe, a secondary and superadded change, and may very plausibly, on Chauffard's theory of splenogenous cirrhosis, be referred to the action of poisons manufactured in the enlarged spleen and conveyed to the liver by the portal vein. In cases that die from accident or from some intercurrent disease the monolobular cirrhosis, described by Hanot, may be seen unobscured by the secondary multilobular cirrhosis which develops in long-standing cases.

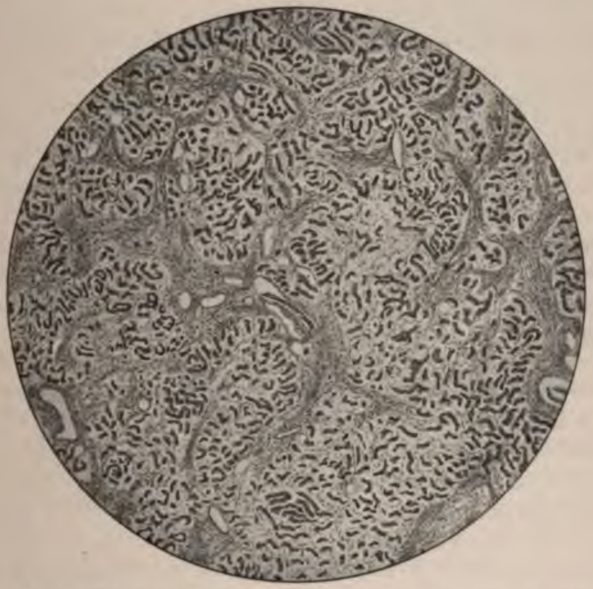

FIG. 37.—DRAWING OF MONOLOBULAR CIRRHOSIS WITH SOME INVASION OF THE LOBULES BY DELICATE CONNECTIVE TISSUE.

The liver cells are shrunken from the effects of the hardening agent (absolute alcohol). × 25.

The connective tissue of the monolobular cirrhosis is delicate and fibrillar, somewhat like neuroglia, and has an open structure. In some parts it invades the lobules and becomes pericellular. As compared with the fibrosis of multilobular cirrhosis it is much less dense, but is more intimately related to the lobules and cells of the liver. The delicate connective tissue contains branching anastomosing elastic fibres, which invade the lobules and form a fine network between the cells. The elastic tissue is derived from the sheaths of the hepatic artery, portal vein, and bile-ducts, and may also spread in from the capsule, where it is normally present. There is less newly formed elastic tissue in biliary cirrhosis than in portal cirrhosis. (Flexner.*)

The existing small bile-ducts show proliferation of their lining epithelium which may block up the lumen and so lead to biliary obstruction; as a result, the bile capillaries often contain plugs of inspissated bile. Around the inflamed bile-ducts there is fibrosis.

Pseudobile Canaliculi.—Around the margins of the lobules and in the fibrillar interlobular connective tissue there are columns of small, deeply staining cells. The cells, which surround a potential lumen, are either cubical or elongated so as to lie parallel to the long axis of the column. Occasionally the lumen is dilated, and though ordinarily empty, may contain minute biliary calculi. The columns of cells twist and branch in the neighbourhood of the lobules. Though they are particularly well marked in hypertrophic biliary cirrhosis, and are only exceptionally absent in that disease, their presence cannot in any way be considered diagnostic of it, for they are met with in a large number of other morbid conditions of the liver, such as portal cirrhosis, abscess, acute yellow atrophy, gumma, tuberculosis, etc., which tend to destroy the liver cells or interfere with their functional activity. The histological appearances of the so-called new bile-ducts are the same in all these various conditions and differ from normal bile-ducts in that there is either a complete absence of a covering of elastic fibres or a very imperfect development of this tissue around them. (Flexner.†)

A great deal of discussion has taken place as to their nature and origin. (*Vide* Portal Cirrhosis, p. 205.) They have been thought to be the pre-existing bile-ducts brought into greater prominence, to be new bile-ducts derived from the ducts normally present, compressed liver cells surrounded by fibrous tissue, or, lastly, young liver cells—the result of compensatory hyperplasia of the hepatic cells at the periphery of the lobules. The question is discussed on page 206, and the most probable conclusion is that they are the result of compensatory hyperplasia of the liver cells.

Hanot and Gastou ‡ regard these so-called new bile-ducts as the first results of irritation on the liver cells, and explain their frequency in hypertrophic biliary cirrhosis as a direct consequence of the exacerbations in the course of the disease.

The liver cells are for a long period extremely well preserved, and when the patient dies from some other cause, do not show the fatty and degenerative changes seen in portal cirrhosis. In many cases acute degenerative or toxic changes occur shortly before death.

Relation of Banti's Disease to Hypertrophic Biliary Cirrhosis.—In chronic splenic anæmia a terminal multilobular cirrhosis may supervene, probably as the result of poisons manufactured in the spleen; this is called Banti's disease. Hypertrophic biliary cirrhosis is essentially monolobular, but in the late stages a secondary multilobular cirrhosis, probably of splenic origin and like that of Banti's disease, may supervene.

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* Flexner: University Medical Magazine, Philadelphia, Nov., 1900, p. 614.

† Flexner: University Med. Magazine, Philadelphia, 1900, p. 617.

‡ Hanot et Gastou: Soc. de biolog., July 15, 1893, p. 741.

The Spleen.—The spleen is enlarged to a much greater degree than in portal cirrhosis; its weight commonly varies between 15 and 40 ounces, but may scale considerably more. The organ may thus weigh twice to six times its normal weight, while the liver is seldom more than twice or three times its ordinary weight. The spleen is therefore relatively more increased in weight than the liver. In some rare cases the spleen is absolutely bigger and heavier than the liver; this is more likely to be met with in children than in adults. To this condition Gilbert[*] has applied the somewhat cumbrous term hypersplenomegalic hypertrophic biliary cirrhosis.

In F. Taylor's[†] case the spleen weighed 87½ ounces and the liver 40 ounces, and in a case recorded by Milian and Landrieux[‡] the spleen weighed 94½ ounces and the liver 65½ ounces.

In a case of hypertrophic biliary cirrhosis of very chronic nature, in which jaundice, enlargement of the spleen down to the umbilicus, and clubbing of the fingers were noticed seven years before death, the liver weighed 65 ounces and the spleen 77 ounces. (H. Roger Smith.[§])

There are frequently perisplenic adhesions from local peritonitis and thickening of the capsule with local exaggerations of this change or lamellar fibromata. In uncomplicated cases, *i. e.*, where death is not the result of a secondary and acute infection, the spleen is firmer than natural.

Microscopically there is fibrosis with distension of the sinuses with blood. The Malpighian bodies in an early stage are hyperæmic, while later they may undergo fibrotic atrophy, a process which occurs in other chronic toxæmic processes, and has been obtained experimentally by Pilliet[‖] as a result of poisoning by metatoluylendiamine, paraphenylene, and nitrate of soda. There is also some endothelial hyperplasia in the splenic pulp.

The **lymphatic glands** in the portal fissure are sometimes enlarged, but are so soft that they do not exert pressure on the bile-ducts. They are dark in colour and œdematous; microscopically there are fibrosis and pigmentation. The pigment is probably derived from destruction of the red blood corpuscles (hæmolysis), but differs from the pigmentation of general hæmochromatosis in not involving the liver and spleen. The lymphatic glands around the pancreas may also be affected in a similar manner, and in exceptional instances glandular enlargement has been detected in distant parts of the body, such as the groin, axilla, mediastinum, and neck. (Popoff.[**])

The **alimentary canal** is usually free from signs of past inflammation. Hanot noted that the duodenum in the region of the biliary papilla was not affected by catarrh; Debove's experience, however, is rather in the opposite direction.

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[*] Gilbert: La Semaine Médicale, 1900, p. 124.
[†] Taylor, F.: Guy's Hosp. Reports, vol. liv, p. 5.
[‡] Milian et Landrieux: La Semaine Médicale, 1900, p. 124.
[§] Smith, H. Roger: Trans. Clin. Soc., vol. xxxi, p. 264.
[‖] Pilliet: Compt. rend. soc. de biolog., Paris, 1894, p. 331.
[**] Popoff: Sovrem klin., 1895, St. Petersburg.

The pancreas, as a rule, is not increased in size or weight, but it is far from normal. It is indurated and may be united by adhesions to neighbouring organs. There is an intimate fibrosis of an embryonic type spreading from the ducts. In addition to this periductular fibrosis there is some proliferation of the cells lining the ducts and fatty degeneration of the cells of the acini. (Lefas.*) In exceptional cases, as in Guillain's † hypertrophic cirrhosis of the liver and pancreas with extreme splenic enlargement, the pancreas may be enlarged.

The kidneys, except for bile-staining, are healthy and may show hypertrophy. (Milian.‡) All the organs are bile-stained.

CLINICAL PICTURE.

The onset may be gradual, and before jaundice sets in malaise, loss of strength, and, in some cases, dyspepsia and abdominal pain may be noticed. Occasionally pain is first noticed in the left hypochondrium, and physical examination shows that there is considerable enlargement of the spleen. Usually, however, the patient first seeks medical advice and thinks seriously of his condition after the appearance of jaundice. The onset of jaundice may be almost imperceptible; in other cases it may be sudden and be accompanied by gastro-intestinal disturbance, thus resembling catarrhal jaundice, or be accompanied by abdominal pain and some fever, so as to imitate an attack of intermittent hepatic fever due to a calculus in the common bile-duct.

Gilbert § has described three modes of onset: (i) The hepatic, with jaundice and pain over the liver; (ii) the gastro-intestinal, with loss of appetite, sickness, diarrhœa, and abdominal pain, and (iii) the splenic, with pain in the left hypochondrium and enlargement of the organ.

The course of the disease is characteristically slow. For a considerable time—often for years—the general health is fairly maintained in spite of persistent jaundice. From time to time attacks of abdominal pain with fever and increase in the degree of jaundice occur; these exacerbations, like those in pernicious anæmia and in Addison's disease, leave the patient in a deteriorated condition of general health and nutrition. As time goes on the periodic exacerbations become more frequent and the disease makes steady though slow progress; wasting and loss of strength appear and the patient's general condition becomes very unsatisfactory. Death may occur from intercurrent disease, from the gradual development of complete hepatic insufficiency and the resulting toxæmia, or during one of the exacerbations acute degenerative changes in the liver cells may lead to the phenomena of icterus gravis. In the last event jaundice deepens, delirium and nervous symptoms appear, and a "typhoid" or comatose condition ushers in death.

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* Lefas: Archives Générales de Médecine, May, 1900, p. 539.
† Guillain: Revue de Médécine, Sept., 1900, p. 701.
‡ Milian: Bull. Soc. Anat. Paris, 1901, p. 323.
§ Gilbert: La Semaine Médicale, 1900, p. 186.

Symptoms.—The tongue is often furred, but may be clean for long periods. The appetite is sometimes poor, but is frequently normal and in some instances has been very excessive. There is not the same marked distaste for fatty food met with in ordinary obstructive jaundice. Dyspepsia is much less frequent than in portal cirrhosis. Hayem stated that hyperacidity is constant, but Kirikow * examined a number of cases without being able to confirm this. Nausea and vomiting are occasionally present. Hæmatemesis is very seldom met with. It may occur late in the course of the disease as the result of secondary portal cirrhosis and even prove fatal.

Milian † has recorded fatal hæmatemesis from an œsophageal varix.

Attacks of diarrhœa on slight provocation are not uncommon. The motions contain bile; this is a point of distinction between the disease and obstructive jaundice with hepatic enlargement.

In 26 cases collected by Schachmann‡ bile was absent from the fæces in only two. From attacks of intercurrent catarrhal jaundice the stools may be temporarily devoid of bile.

The abdomen is prominent and distended, especially in the upper quadrants, from the large size of the liver and spleen. Some of the distension is due to tympanites and a weakened condition of the abdominal walls. Until late in the course of the disease ascites is absent or only present in slight amount, being then due to intercurrent attacks of perihepatitis and perisplenitis. Towards the termination of the disease ascites may be considerable from the development of secondary portal cirrhosis and concomitant toxæmia. The abdominal distension, which is present more or less throughout the disease, is independent of ascites.

There is a sense of weight in the right hypochondrium and periodic attacks of pain with tenderness over the liver and spleen. These attacks may even suggest biliary colic. There may be little or no enlargement of the subcutaneous veins around the umbilicus, but it cannot be said that this feature of portal cirrhosis is completely absent in hypertrophic biliary cirrhosis. It may develop as the result of superadded portal cirrhosis in the later stages of the disease.

Physical Signs.—*The liver* is much and uniformly enlarged, and smooth and firm to the touch, as a rule, but occasionally slightly irregular from the presence of perihepatitic adhesions. Its dulness often extends upwards to the fourth rib in the right nipple line, and downwards to the umbilicus or even below that point, and as far as the crest of the ilium. The pressure of the enlarged organ pushes the costal arch out. On palpation there is slight general but not any localized tenderness. There is no enlargement of the gall-bladder. The enlargement of the liver is, generally speaking, progressive; it may vary from time to time, and increase in size during the periodic exacerbations of the disease. Late in the disease it sometimes diminishes in bulk from some degree of contraction of the fibrous tissue, probably of that constituting the multilobular cirrhosis.

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* Kirikow: St. Petersburg med. Wochen., Bd. xxvii, S. 357, 1902.
† Milian: La progrès Médical, April 14, 1900.
‡ Schachmann: Thèse de Paris, 1889.

A rare and special form of the disease—atrophic biliary cirrhosis—has been described [*] in which the liver is small, and the symptoms are those of biliary cirrhosis in general, but develop rapidly.

The spleen is very considerably enlarged—much more so than in common cirrhosis. It is more marked in children, in accordance with the fact that its capsule is more distensible than in adults. A special form of hypertrophic biliary cirrhosis has been described by Gilbert and Fournier as the juvenile type, or "cirrhose biliare splenomegalique." The spleen may, indeed, be not only relatively but absolutely heavier than the liver.

Three forms of the disease have been described by Gilbert and Castaigne [†] according to the amount and degree of splenic enlargement:

(I) The ordinary or hepatic type, in which the liver and spleen are both considerably enlarged.

(II) The splenomegalic type, in which the splenic enlargement is the predominant feature. For cases where the spleen is actually larger than the liver Gilbert [‡] has more recently employed the title "hypersplenomegalic biliary cirrhosis."

(III) The hepatomegalic type, where the enlargement of the liver is the predominating feature. Gilbert more recently speaks of this as the microsplenic or asplenomegalic form of biliary cirrhosis. The spleen may not be enlarged.

The splenic enlargement may precede any enlargement of the liver; Boix [§] and Popoff [‖] insist that it always does. Chauffard [**] lays great importance on the time relations between the hepatic and splenic enlargement and divides the cases into three groups:

(I) Where the spleen and liver are simultaneously and equally affected.

(II) Where the spleen is affected first and in a greater degree—metasplenomegalic hypertrophic biliary cirrhosis; the cirrhosis he believes to be secondary to poisons manufactured in the spleen.

(III) Where the liver enlarges first and probably determines the splenic enlargement—presplenomegalic hypertrophic biliary cirrhosis.

The spleen is firm, smooth on the surface, but not so hard as in myelogenous leukæmia. When attacks of inflammation of the capsule supervene, friction may be heard with the stethoscope, and in some instances a soft blowing murmur may be audible over the spleen.

Jaundice is slight at first and becomes more marked as the disease progresses; it is permanent, but varies in degree, being intensified at intervals when exacerbations in the disease occur. After these crises it recedes a little, but, on the whole, slowly progresses. The jaundice may eventually become very dark or green. There may be considerable brown discolouration of the skin, resembling that of Addison's disease. This melanoderma may occur early, before icterus has made its appearance (Roger Smith), but usually it is combined with the icteric staining of the skin. There may be troublesome itching, and from scratching the skin may become covered by an eczematous or lichenous eruption. Long-continued jaundice may lead to the striking lesion of the skin—xanthelasma. I have seen it in a case where moderate jaundice had existed for nine months. It is said that in some cases of otherwise typical hypertrophic biliary cirrhosis jaundice is absent.

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[*] Lereboullet: Les Cirrhoses Biliares, Thèse Paris, 1902, No. 180.

[†] Gilbert and Castaigne: Soc. de biolog., May 20, 1899, p. 403.

[‡] Gilbert: La Semaine Médicale, 1900, p. 154.

[§] Boix: Soc. de biolog., March 12, 1898, p. 297.

[‖] Popoff: Leçons Clinique, St. Petersburg, 1896. Quoted by Boix.

[**] Chauffard: La Semaine Médicale, 1900, p. 176.

Hæmorrhages.—In the later stages of the disease there may be a hæmorrhagic tendency, shown by cutaneous petechiæ, epistaxis, bleeding from the gums and throat, and in exceptional instances hæmoptysis and hæmaturia; hæmatemesis is rare.

Physical Development.—The patients are thin, badly nourished, and when not adults, frequently small for their age. As in a number of other conditions, such as cretinism, hereditary syphilis, and congenital morbus cordis, growth and bodily development may be greatly interfered with and the onset of puberty and in girls menstruation postponed. To this condition the term "infantilism" is applied.[*] The skin is dry; sometimes there is dark-brown pigmentation, suggesting that some other cause than jaundice is at work. Œdema of the feet may occur in the late stages.

Clubbing of the Fingers.—In some cases of long standing a peculiar change, consisting in clubbing of the terminal phalanges of the fingers and toes, has been observed. The terminal phalanges may be expanded and broadened so that the finger resembles a spoon or even a pendulum. The nails may be overcurved at the same time and may be longitudinally striated; in extreme instances the nails have been compared to a parrot's beak. This change is much the same as that seen in congenital morbus cordis and chronic lung disease, and sometimes spoken of as "Hippocratic fingers." Its occurrence in biliary cirrhosis is rare, though Gilbert and Lereboullet [†] were able to refer to 40 cases in 1901. It is met with more often in children, in whom it was first described by Gilbert and Fournier,[‡] than in adults. Examination with the x-rays shows that there is no bony enlargement of the terminal phalanges (F. Taylor,[§] Boutron [‖]). The clubbing is due to thickening of the soft tissues, and on the analogy of its occurrence in bronchiectasis and empyema the change is probably due to the action of toxines. But although the change resembles Marie's hypertrophic pulmonary osteo-arthropathy in a minor degree, it is not associated with intra-thoracic disease, and there is no reason to think that it is due to embarrassment of the right lung by the upward pressure of the enlarged liver. Neither is it confined to this form of hepatic disease, for it was well marked in a boy aged seventeen, under the care of my colleague, Dr. Ewart, with syphilitic stricture of the bile-ducts (*vide* Fig. 38), and in very rare instances it has occurred in portal cirrhosis. In a few cases the bulbous or "Hippocratic" fingers have been found associated with perforating ulcer of the foot, and neuritis, in hypertrophic biliary cirrhosis.

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[*] For references on the subject of infantilism see Hutinel: Gaz. hebdom. de Méd. et de chirurg., 1902, p. 37; H. Meige: Gaz. des Hôp. Paris, 1902, p. 207.

[†] Gilbert and Lereboullet: Gaz. hebd. de Méd. et de chirurg., 1902, p. 1.

[‡] Gilbert and Fournier: Rev. Mens. de Malad. de l'enfance, July, 1895, p. 309.

[§] Taylor, F.: Guy's Hospital Reports, vol. liv, p. 13.

[‖] Boutron: Thèse de Paris, 1899, No. 513.

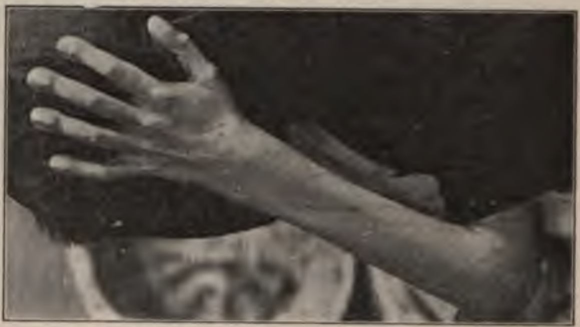

Fig. 38.—Photograph showing Bulbous Fingers Resembling those seen in Hypertrophic Biliary Cirrhosis. From a Case of Tardive Hereditary Syphilis with Stricture of the Hepatic Ducts. (Photograph by Dr. H. G. Drake-Brockman.)

Reference for the subject of clubbed fingers in biliary cirrhosis may also be made to the following sources: Roger-Smith: Trans. Clinic. Soc., vol. xxxi, p. 258; F. Taylor: Guy's Hospital Reports, vol. liv; Parmentier and Castaigne: La Sem. méd., 1901, p. 94; Rhorassandri: Thèse Paris, 1900, No. 160.

Arthritis, etc.—Enlargement of the ends of the bones, synovitis, and pain in the joints, so-called biliary rheumatism, has been described by Gilbert and Fournier. The enlargement of the ends of the bones is an osteopathy analogous to Marie's pulmonary form.

In a man aged twenty-three years, who rapidly developed the clinical picture of hypertrophic biliary cirrhosis, a remarkable attitude of the body appeared. The right shoulder, pelvis, and hip were depressed without any spinal curvature to account for it. The patient himself was unconscious of the condition and could by an effort temporarily correct it. Sicard and Remlinger * thought that the enlarged liver might possibly have some part in bringing about this curious attitude, though it had not been noticed in cases with much bigger livers.

Nervous System.—As a rule, there is nothing special to note with regard to the nervous system. As the result of jaundice there may be some mental depression and some failure of memory, while occasionally there may be emotional disturbance. Marked drowsiness is not a very rare symptom. In the terminal stages toxæmic symptoms, such as delirium, coma, and convulsions, are seen. I have seen definite peripheral neuritis with numbness of the fingers, but this appears to be quite unusual.

The *heart* tends to dilate, and a systolic mitral murmur or hæmic murmurs may be heard at some time during the course of the disease. The *pulse* is regular and of fair tension. There is no slowing.

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* Sicard and Remlinger: Rev. de Méd., Sept., 1897, p. 693.

Blood.—There is anæmia of a secondary character, the red corpuscles being usually reduced to between 4,500,000 and 2,200,000 and the hæmoglobin value being below 1.

Observations by Hayem and by Cabot[*] have shown that in exceptional instances the amount of hæmoglobin may be relatively excessive. Thus in Hayem's case there were 1,884,000 red corpuscles with 50 per cent. of hæmoglobin; the diagnosis was confirmed by an autopsy. It must be borne in mind, as pointed out by Cabot, that the presence of bile in the blood renders the estimation of hæmoglobin unsatisfactory.

There is no poikilocytosis (Milian [†]); the blood is less coagulable than in health. The question as to the presence or absence of leucocytosis is not settled. Hanot stated that leucocytosis was present, but this statement has not been universally confirmed. It appears that leucocytosis is not constant, and may be absent. When present, it is not very marked, varying between 9000 and 15,000, and is due to an increase in the polymorphonuclears (Milian [‡]).

Hanot and Meunier [§] found leucocytosis in 5 cases and Cabot [‖] in 4 out of 6 cases; DaCosta [**] in 2 out of 6. It was absent in cases reported by Taylor, and Milian and Kirikow [††] found that leucocytosis was only present when there were complications, and that a normal count or leucopenia was the rule. Bigart's [‡‡] observation of increase in the number of mast cells appears to be quite unique and may have been due to some independent factor.

Respiratory System.—There may be shortness of breath, due to the upward displacement of the diaphragm, anæmia, and cardiac dilatation. Occasionally, as part of the general hæmorrhagic tendency, hæmoptysis may occur. Cough is sometimes persistent, and suggestive of tuberculosis, but tubercle bacilli are very rarely found in the sputum.

Urine.—The quantity passed is subject to considerable variations; usually it is increased in amount, but during the exacerbations it may be diminished. Milian [§§] lays stress on polyuria as a characteristic feature. It is high-coloured and rich in urinary pigments. Urobilin and indican are both occasionally present. Bile pigment is practically always present. Unlike the concentrated urine of portal cirrhosis, there is little tendency to deposit urates.

There is usually no albuminuria; when present, it has been noticed to be intermittent. Casts, if carefully looked for, are nearly always found; their presence appears to depend on the jaundice. The amount of urea varies; it may be normal or may at times be diminished. Glycosuria does not occur. Owing to the fact that the liver cells preserve their nutrition for a considerable period, alimentary glycosuria, induced by giving three ounces of sugar on an empty stomach, cannot be produced in most cases.

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[*] Cabot: Examination of the Blood, p. 250.

[†] Milian: Bull. Soc. Anat. Paris, 1903, p. 13.

[‡] Milian: Bull. Soc. Anat. Paris, 1903. p. 13.

[§] Hanot and Meunier: Compt. Rend. Soc. biolog., 1895, tome ii, p. 49.

[‖] Cabot: Examination of the Blood, p. 250.

[**] DaCosta: Clinical Hæmatology, p. 352.

[††] Kirikow: Zeitschrift f. klin. Med., Bd. xxxvi, S. 444. Kirikow and Korobkow: Russ. Archiv f. Path., klin. Med., u. Bakt., St. Petersburg, 1902.

[‡‡] Bigart: Soc. de Biolog., Dec. 27, 1902.

[§§] Milian: Bull. Soc. Anat. Paris, 1901, p. 323.

The toxicity of the urine is said to be feeble, and this has been used as an argument against the view that hypertrophic biliary cirrhosis is primarily due to a general hæmic infection. The freezing-point of the urine, or its cryoscopic value, has been found to be high (Ferrannini*).

TERMINATION.

In uncomplicated cases the disease slowly progresses until a fatal toxæmic condition results from destruction of the liver cells. The "typhoid" state develops and the patient becomes more jaundiced, drowsy, and passes into coma. During this stage ascites may develop, or in rare instances death may be precipitated by fatal gastro-intestinal hæmorrhage, as, for example, in the following case:

A married, childless woman, aged thirty-two, who had had one miscarriage, was admitted under my colleague, Dr. Penrose, at St. George's Hospital with jaundice of four months' duration, a greatly enlarged and tender liver, enlarged spleen and no ascites, but a history of several attacks of hæmatemesis. The urine was bile-stained and contained a trace of albumin. There were no distended abdominal veins. There was a systolic murmur over the pulmonary artery. There was no definite history of alcoholism, but it was suspected. A few days after admission hæmatemesis recurred and was often repeated; the patient became delirious and finally comatose, and in spite of being bled from one arm to about a pint and transfused to two pints in the other arm, she died. At the autopsy there was no ascites. The liver, weight 7 pounds 9 ounces, was slightly irregular on the surface and on section showed fine cirrhosis; it was deeply bile-stained. The bile-ducts were pervious and the gall-bladder contained dark bile but no calculi. Portal vein healthy. Microscopically, cirrhosis was comparatively slight; liver cells very fatty, no signs of acute atrophy, numerous so-called new bile-ducts. Cirrhosis almost unilobular.

As in most chronic diseases death may be due to some acute infection; thus, pneumonia, erysipelas, or peritonitis may carry the patient off. Erysipelas is very prone to attack patients with chronic jaundice, and, from their want of resistance, to prove fatal; but in hypertrophic biliary cirrhosis erysipelas, though a severe complication, is not necessarily fatal. If acute infection falls on the liver itself, the symptoms of icterus gravis develop.

DIAGNOSIS.

Chronic jaundice without complete biliary obstruction, as shown by the colour of the fæces; the occurrence of periodic exacerbations, and considerable enlargement of the liver and spleen, without any evidence of cholelithiasis, in a young person, are the essential points on which to base a diagnosis of hypertrophic biliary cirrhosis.

Differential Diagnosis.—In cases of *portal cirrhosis* with big livers and intercurrent jaundice the diagnosis depends on the jaundice being transitory and not permanent, on the comparatively slight degree of splenic enlargement, and on the history and presence of signs of common cirrhosis. It cannot, however, be maintained that the two diseases (portal and biliary cirrhosis) are always distinct, either anatomically or clinically. Sometimes they are combined, and not infrequently the two diseases overlap in the same way as the parenchymatous and interstitial forms of nephritis.

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* Ferrannini: Centralblatt f. inn. Med., March 14, 1903.

The following case presented features of both diseases, but it might also be interpreted as a case of portal cirrhosis with acute and recent inflammation of the intra-hepatic bile-ducts:

A man aged forty-seven died in St. George's Hospital; he had had hæmatemesis and ascites which required tapping; for the last three weeks of his life he was delirious and jaundiced. His liver weighed 50 ounces and was typically hobnailed; microscopically it showed multilobular and monolobular cirrhosis, a large number of pseudobile canaliculi, and microscopic calculi in the bile capillaries. The spleen weighed 18 ounces.

In *hæmochromatosis*, a condition in which there is widespread pigmentation of the body with secondary cirrhosis of the liver and pancreas, the liver is enlarged and some of the symptoms resemble those of hypertrophic biliary cirrhosis. The skin, however, though pigmented, is not jaundiced, and in five-sixths of the cases there is glycosuria (bronzed diabetes).

In cases of *obstructive jaundice* the liver may be enlarged and swollen from retained bile; but this condition differs from hypertrophic biliary cirrhosis in the absence of bile from the fæces, in the fact that there is no splenic enlargement, while in many cases the presence of an enlarged gall-bladder can be made out when the common bile-duct is obstructed.

Chronic jaunidce due to a calculus in the common duct may imitate hypertrophic biliary cirrhosis in the periodic attacks of intermittent hepatic fever, and in the fact that the stools are not necessarily devoid of bile. Calculi usually occur later in life than biliary cirrhosis, the periodic attacks of pain are more severe than in hypertrophic biliary cirrhosis, and the spleen is either not enlarged at all or only in a slight degree.

In some cases of *hydatid cysts in the liver with jaundice* the resemblance to biliary cirrhosis is considerable. In ordinary hydatid disease the spleen is not enlarged, the periodic attacks of fever and pain are absent, and jaundice when present is either due to rupture of a cyst into the duct, in which case there is usually continued fever, or due to pressure on the larger ducts with complete exclusion of bile from the intestines.

In *prolonged catarrhal jaundice* the spleen is either not enlarged or very slightly, and bile is absent from the fæces. In cases of *chronic infectious jaundice* the condition is indistinguishable from that of hypertrophic biliary cirrhosis, except when recovery occurs; in other words, the symptoms of the two diseases are practically identical, though their results and course are different.

In *Weil's disease* the clinical course is rapid and acute, whereas in hypertrophic biliary cirrhosis it is a matter of years, not of days.

Malaria, which has in the past been erroneously regarded as the cause of hypertrophic biliary cirrhosis, can be eliminated by examination of the blood and by the failure of quinine to affect the course of the disease.

Some rather exceptional cases of *syphilitic disease of the liver with* *chronic jaundice* and very considerable enlargement of the liver and spleen may imitate hypertrophic biliary cirrhosis. Syphilitic lesions elsewhere, albuminuria as pointing to lardaceous disease as the cause of splenic enlargement, irregularity of the surface of the liver from gummata, the presence of enlarged veins near the umbilicus, and the beneficial effects of antisyphilitic treatment point to syphilis. Another point, which, however, is of rather doubtful value, is the absence of leucocytosis in syphilis and its presence in hypertrophic biliary cirrhosis.

In the following case the presence of gummata on the limbs pointed to syphilis, but in other respects the features closely resembled those of Gilbert and Fournier's splenomegalic type of hypertrophic biliary cirrhosis:

A boy aged seventeen years was frequently under the care of my colleague, Dr. Ewart, with chronic jaundice, no ascites, great enlargement of the liver and spleen, both of which were smooth, clubbing of the fingers, and gummata on the limbs and head.* He died of erysipelas; the liver, which weighed 5 pounds, was jaundiced and consisted almost entirely of an hypertrophied left lobe; the right lobe showed numerous cicatrices and was atrophied. The left hepatic duct was obliterated by scar tissue while bile entered the gall-bladder and intestines by the right hepatic duct. There was no cirrhosis of the left lobe. The spleen weighed 2 pounds 13 ounces. There was no lardaceous change in any of the organs of the body.

From Banti's Disease.—As already mentioned, there is a gradual transition between (*a*) cases of so-called metasplenomegalic biliary cirrhosis, in which the splenic enlargement precedes any manifest change in the liver, and (*b*) cases of chronic splenic anæmia which eventually develop a terminal cirrhosis of the liver and jaundice—so-called Banti's disease. To distinguish between the two a reliable history is necessary. In chronic splenic anæmia there is marked anæmia of the chlorotic type, an absence of any leucocytosis or even a diminution in their number (leucopenia), and recurrent gastro-intestinal hæmorrhages before the development of jaundice, while in metasplenomegalic biliary cirrhosis there would be practically an absence of symptoms during the period in which splenic enlargement (splenomegaly) was the only physical sign.

DURATION.

Though the disease must be regarded as incurable, it is essentially chronic, and jaundice may exist for ten years or even longer. The average duration is about five years. In a few instances the disease runs an acute course, and then proves fatal within two years.

PROGNOSIS.

The prognosis is bad, since the disease is incurable. But it is often extremely slow in its progress and patients may retain fair strength for years. Careful treatment and supervision may be followed by improvement, and the outlook depends on the surroundings of the patient. An easy life in a healthy locality will prolong life, while overwork, exposure to cold and wet, and unsanitary conditions will surely lead to deterioration.

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* The case was described by W. S. Lazarus Barlow: Trans. Path. Soc., vol. l, p. 158.

The patient's general nutrition has, of course, an important bearing on the prognosis. Wasting and the recurrence of exacerbations and hæmorrhages at more frequent intervals show that the disease is advancing towards its termination. The incidence of complications, such as pneumonia, peritonitis, or erysipelas, at once makes the outlook very serious. Erysipelas may be recovered from in cases where the urinary secretion is well maintained. Clubbing of the fingers, though a rare condition, is only met with in long-standing cases, and is an indication that the course of the disease has been slow.

TREATMENT.

The general lines of treatment are the same as those in portal cirrhosis. In certain points there are differences: thus, a more generous diet may be allowed in this disease than in portal cirrhosis, while itching of the skin due to jaundice is more, and ascites and hæmatemesis less, likely to require treatment than in ordinary cirrhosis. In the early stages an attempt may be made to put the patient in more healthy surroundings and to remove him from the conditions, among which the water-supply may play a part, that favoured the onset of the disease. Fresh air is important, but exposure to chills, and especially to cold and damp weather, should be avoided and the patient should be warmly clad. A course at Homburg, Ems, Neuenahr, Kissingen, Vichy, Vals, Harrogate, may be tried. If the patient goes to Carlsbad, the course must be comparatively mild.

Diet.—It is important that the diet should be simple and nourishing. Irritating and unduly stimulating articles of food should be carefully excluded. Milk should be given freely, eggs, bread and butter, simple puddings, fish, and occasionally meat may all be taken. Alcohol must be avoided; and if taken at all, must be in small quantities and well diluted. Water should be taken freely, but it will be advisable to have it boiled when the patient is still living in the house where the disease developed.

Intestinal fermentation and putrefaction should be prevented by careful dieting, correction of constipation, and by minute doses of calomel ($\frac{1}{40}$–$\frac{1}{20}$ of a grain) three times a day; rather larger doses ($\frac{1}{6}$–$\frac{1}{2}$ grain) may be employed in single doses to combine its antiseptic and purgative properties. Calomel is preferable to salol, β-naphthol, betol, and the synthetic intestinal antiseptics. Saline purgatives, such as sulphate of magnesium and sulphate of soda in combination, are also useful in preventing intestinal fermentation, while mineral waters may be employed with the same object. It has been suggested by Parkes Weber * that an attempt should be made to treat the catarrhal condition of the small bile-ducts by drugs which, when excreted into the intra-hepatic ducts, should disinfect the ducts in the same way that urotropin and salol disinfect the urinary tract. Possibly salicylates or some similar drug may do good in this way.

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* Weber, F. Parkes: Edinburgh Med. Journ., new series, vol. xiv, p. 14, Aug., 1903.

Itching of the skin may be treated externally by warm baths or fomentations with carbolic acid lotions; while internally chloride of calcium in 20-gr. doses or antipyrin, grs. v–x, may be employed. Small hypodermic injections of pilocarpine have also been recommended.

Surgical Treatment.—Terrier[*] and Delageniere[†] have drained the gall-bladder in a number of cases and with very good results. Thus, in 13 cases tabulated by Maurice Guillot[‡] 10 were cured; Greenough[§] adds 4 cases, making up a total of 17 cases, of which 13 were relieved. It is not certain that all the cases were of the same type; some of them may possibly have been examples of chronic infective cholecystitis and cholangitis and not genuine cases of biliary cirrhosis (*vide* Michaux[‖]), but it appears that many of them were examples of hypertrophic biliary cirrhosis. The drainage of the gall-bladder was continued for periods varying from ten days to three months, and in some instances the bile, which was at first infected, became aseptic.

OBSTRUCTIVE BILIARY CIRRHOSIS.

By obstructive biliary cirrhosis is meant a fibrosis spreading from the bile-ducts around the lobules of the liver and due to obstruction of the large bile-ducts.

History.—The conception of cirrhosis due to biliary obstruction was first prominently brought forward by Charcot and Gombault[**] in 1876, though two years previously Wickham Legg[††] in England had described a clinical case with full pathological details. In 1882 Mangelsdorf[‡‡] collected 184 cases, and in 1901 W. W. Ford[§§] and in 1903 Weber[‖‖] argued in favour of the truth of this sequence of pathological events.

EXPERIMENTAL LIGATURE OF THE BILE-DUCTS.

As bearing on the production of obstructive biliary cirrhosis, numerous experiments have been performed in which the bile-ducts have been ligatured and the liver subsequently examined for any fibrosis. The conclusions arrived at, as will be seen, are by no means uniform.

Meyer[***] in 1872 ligatured the common bile-duct of cats and produced dilatation of the bile-ducts with intralobular and extralobular fibrosis. Charcot and

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[*] Terrier: Rev. de chirurg., tome xii, p. 553, 1892.

[†] Delageniere: Archiv provinc de Chirurg., 1897.

[‡] Guillot, M.: Gaz. hebdom. de Méd. et de chirurg., Jan. 16, 1902, p. 69.

[§] Greenough: American Journ. of Med. Sciences, vol. cxxiv, p. 979, Dec., 1902.

[‖] Michaux: Rev. de chirurg., tome xxiii, p. 126.

[**] Charcot and Gombault: Archiv de Physiol. norm. et. path., 1876, 2d series, t. iii, p. 272.

[††] Wickham Legg: St. Bartholomew's Hosp. Reports, 1873.

[‡‡] Mangelsdorf: Deutsch. Archiv f. klin. Med., Bd. xxxi, S. 522, 1882.

[§§] Ford, W. W.: American Journ. Med. Sciences, vol. cxxi, p. 60.

[‖‖] Weber, F. P.: Trans. Path. Soc., vol. liv, p. 103, 1903.

[***] Meyer: Med. Jahrb., Vienna, 1872.

Gombault's[*] (1876) results are well known and, like the earlier experiments of Wickham Legg[†] (1873), showed that ligature of the duct led to dilatation of the intra-hepatic ducts with fibrosis which surrounded the individual hepatic lobules (insular cirrhosis) and spread into their substance (intralobular cirrhosis). The lobules tended to undergo atrophy, while numerous newly formed bile-ducts in the perilobular tissue passed by a gradual transition into the liver cells at the margin of the lobule. Somewhat similar results were obtained by Chambard, and by Foa and Salvioli. Charcot and Gombault referred these changes to the irritating properties of the retained bile, and, indeed, incidentally mention that the bile contained "vibrios." Maffucci[‡] also induced cirrhosis as the result of ligature of the bile-duct.

These results were obtained before the days of antiseptics, and it has often been urged that the cirrhosis was due, not to mechanical pressure and irritation exerted by the retained bile, but to accidental infection. Thus Steinhaus[§] found that after ligature of the bile-ducts in guinea-pigs, who were killed at periods varying from six hours to ten days, no interstitial hepatitis was produced unless septic infection occurred. The interval of ten days is very short, but as most of the animals died within a fortnight after ligature of the common duct, this was unavoidable. In order to keep animals alive longer Josselin de Jong[‖] ligatured individual branches of the hepatic duct instead of the common bile-duct and obtained much the same results as Steinhaus. Similar experiments in the hands of Nasse,[**] and of Vaughan Harley and Barratt,[††] showed that intralobular fibrosis resulted. The latter observers ligatured the left hepatic duct in cats and kept them alive for four to sixteen months, and in dogs without any jaundice resulting; microscopic sections of the left and of the healthy right lobe could then be compared. The changes observed were not absolutely constant, but in many instances well-marked interlobular fibrosis, hyperplasia of the interlobular bile-ducts, and atrophy of the hepatic lobules, beginning at the periphery, were present in the area of the liver corresponding to the ligatured bile-duct. It is interesting to note that Hanot and Gastou[‡‡] in 1893 explained the appearance of so-called new bile-ducts after aseptic ligature of the bile-duct as an irritative lesion of the liver cells in response to poisonous bodies absorbed from the bowel, where excessive fermentation depending on the absence of bile had taken place.

Ligature of the common duct in frogs, guinea-pigs, and rabbits (Lahousse[§§]) under antiseptic precautions gave rise to some fibrosis; other observers (Beloussow,[‖‖] Gerhardt[***]) have obtained similar results. There is thus very considerable difference of opinion as to whether fibrosis is produced or not. In some cases where the ligature is applied to the duct near the duodenum the part of the duct above the ligature may contain micro-organisms, so that although the ligature itself is aseptic, the conditions are complicated. Lamacq[†††] points out that in dogs the liver may normally show infective nodules. His results show that when sepsis is avoided ligature leads to necrosis of the liver cells in rabbits when the bile pressure is relatively high, but that in dogs necrosis is rare and when present not marked. No leucocytic infiltration or fibrosis occurred around the areas of necrosis and no proliferation of bile-ducts. The same results were obtained by Ribadeau-Dumas and Lucéne[‡‡‡] in guinea-pigs.

To sum up the effects of ligature of the bile-ducts: fibrosis may be absent, it may be present and be due to infection, or may, even where infection is absent, be found in varying degrees. This fibrosis following aseptic ligature may be explained in several ways: it may be regarded merely as a fibrosis replacement, perhaps more apparent than real. In cases such as Nasse's and Harley's and Barratt's, where one hepatic duct is ligatured and where the fibrosis is limited to the corresponding part of the liver, this may be the explanation. Harley and Barratt, however, referred the fibrosis to the continued slight irritation of the bile. In other instances the cirrhosis may be due to toxic influences which are brought into existence by failure of the liver properly to perform its antitoxic function of stopping and destroying poisons brought to it by the blood, especially that of the portal vein; in such an event the poisons would reach the liver a second time by the hepatic artery. Or, again, in cases where the common bile-duct is tied the cirrhosis may be due to poisons absorbed from the alimentary canal, where, as the result of interference with the flow of bile, fermentation and putrefaction have been excessive. Lastly, the fibrosis may be entirely independent of ligature of the bile-ducts and due to extrinsic causes developing after the duct has been ligatured.

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[*] Charcot and Gombault: Archiv de Physiol. norm. et path., 2d series, t. iii, p. 272, 1876.

[†] Legg, W.: St. Bart.'s Hosp. Reports, vol. ix, p. 161, 1873.

[‡] Maffucci: Giornal. Internaz. della Scien. Med., 1882, p. 889.

[§] Steinhaus: Archiv f. exper. Path. u. Pharm., Bd. xxviii, S. 432, 1891.

[‖] Josselin de Jong: Inaug. Diss., Leyden, 1894. Quoted by Harley and Barratt.

[**] Nasse: La Semaine Médicale, 1894, p. 202.

[††] V. Harley and Barratt: Brit. Med. Journ., 1898, vol. ii, p. 14, 1743. Journ. Path. and Bact., vol. vii, p. 203, 1901.

[‡‡] Hanot et Gastou: Soc. de biolog., July 15, 1893, p. 741.

[§§] Lahousse: Archiv de biolog., vii, p. 187.

[‖‖] Beloussow: Archiv f. experiment. Path. u. Pharmak., 1881.

[***] Gerhardt: Archiv f. experiment. Path. u. Pharmak., 1892.

[†††] Lamacq: Archiv de Med. expériment. et d'anat. path., Nov., 1897.

[‡‡‡] Archiv de Med. expériment. et d'anat. path., tome xvi, p. 191, 1904.

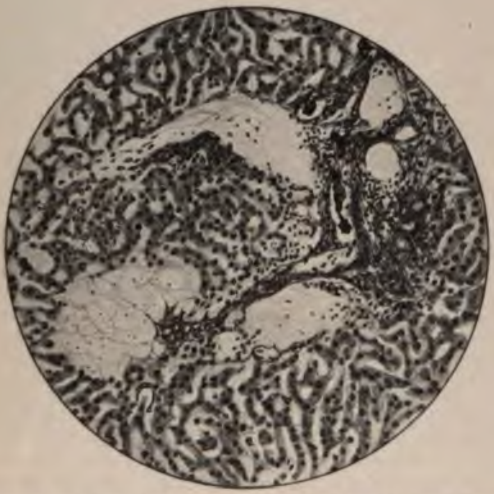

FIG. 39.—FOCAL NECROSIS DUE TO BILIARY OBSTRUCTION. FROM A GUINEA-PIG WHOSE BILE-DUCT WAS COMPRESSED BY A CYST

The pale areas show complete necrosis of the liver cells; there is some small-cell infiltration around the portal space. The bile-ducts contained inspissated bile. (From a specimen kindly lent by Dr. J. H. Drysdale.)

INCIDENCE.

The statistics of Mangelsdorf [*] showed that up to 1882 the published cases of cirrhosis which could be ascribed to biliary obstruction numbered 184; between 1882 and 1900 W. W. Ford [†] collected 21 more and added 3 fresh examples. From his 21 cases collected from literature 10 may be deducted, since 9 belong to the group of congenital obliteration of the ducts and one was an example of congenital cystic disease of the liver. Cases of cirrhosis due to biliary obstruction are therefore not often described. The general opinion as voiced by Osler,[‡] Sharkey,[§] and Hale

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[*] Mangelsdorf: Deut. Archiv f. klin. Med., Bd. xxxi, S. 522.

[†] Ford, W. W.: American Journ. Med. Sciences, vol. cxxi, p. 60.

[‡] Osler, W.: Practice of Medicine, p. 570, ed. iv.

[§] Sharkey: St. Thomas' Hospital Reports, vol. xviii, p. 245.

White * is that mechanical biliary obstruction seldom or never causes genuine cirrhosis, and that although fibrosis may be detected on microscopic examination, it is not of any clinical or practical significance.

EFFECTS OF BILIARY OBSTRUCTION ON THE HUMAN LIVER.

The facts observed in the human subject, like those obtained by experimental work on animals, are not uniform, but there is very little evidence to support the view that biliary obstruction *per se* causes cirrhosis. When the common bile-duct is completely occluded from without, for example, by malignant disease of the head of the pancreas, there is dilatation of the ducts, but as a rule little or no fibrosis, while the liver cells are degenerated, atrophied, and occupied by bile pigment. The liver substance is atrophied and the organ is in a condition comparable to that of hydronephrosis. It is somewhat remarkable that manifest microbic infection does not more often occur, since the biliary stagnation must dispose to infection by micro-organisms reaching the liver by the blood-stream.

Malignant disease of the pancreas with complete biliary obstruction is not a rare disease, but it is remarkable how it is hardly ever associated with cirrhosis of the liver. If biliary obstruction *per se* produced fibrosis of the liver, the association should be often seen. The cases are so few that it seems possible that when hepatic cirrhosis and malignant disease of the pancreas are found in the same person, the cirrhosis was the older lesion and was latent, and that the growth in the pancreas developed subsequently.

Maffucci † and Legrand ‡ have recorded cases where these two conditions were associated.

In addition to the possibility that bacterial infection of the dilated bile-ducts, when obstructed by the pressure of a tumor from without, may occur from the blood-stream, it must be remembered that complete obstruction prevents bile entering the duodenum. In the absence of bile from the intestine putrefactive and fermentative processes in the bowel would tend to become excessive and might lead to the production of poisons, which, when carried to the liver, might be expected to set up the ordinary portal or multilobular cirrhosis. This change would, indeed, in all probability more often be met with, were it not that the liver, being flooded with bile, which has acquired toxic properties, as shown by the focal necroses of the liver cells, is incapable of any reaction.

The cirrhosis of the liver found in association with congenital obliteration of the bile-ducts has been regarded by Ford as secondary to the biliary obstruction and as a good example of obstructive biliary cirrhosis. It is, however, quite as reasonable to believe that the process starts in the smaller ducts, where it sets up pericholangitic fibrosis and then spreads to the larger ducts and gall-bladder, where it sets up obliterative cholangitis and cholecystitis.

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* Hale White: Guy's Hospital Gaz., May 28, 1898. Brit. Med. Journ., 1903, vol. i, p. 534.

† Maffucci: Quoted by Ford, American Journ. Med. Sciences, Jan., 1901.

‡ Legrand: Rev. de Méd., 1889, p. 165.

On the other hand, when a gall-stone is lodged in the common bile-duct, the results are not so constant; sometimes the changes are the same as in aseptic closure of the common duct, but in other instances there are cholangitis and pericholangitis, which, if the process is chronic, result in fibrosis around the ducts. Litten thought that rough and angular calculi were much more likely than smooth round stones to set up cholangitis and fibrosis. In long-standing cases the liver cells undergo widespread degeneration and atrophy and the amount of fibrosis may be very considerable.

Mangelsdorf tabulated 54 cases of hepatic cirrhosis associated with gall-stones, in 16 of which calculi were found in the ducts. Parkes Weber * has recently collected 12 cases of biliary cirrhosis from obstruction of the larger ducts by gall-stones.

Hypertrophic biliary cirrhosis has sometimes been found in association with gall-stones, but it is quite reasonable to think that the gall-stones are secondary to cholangitis and not the primary morbid factor.† The association of impacted gall-stones and hypertrophic biliary cirrhosis must be extremely rare, since Naunyn ‡ has not met with it. There seems to be very little doubt that the factor which determines fibrosis around the intra-hepatic ducts in gall-stone obstruction is bacterial infection. As the result of biliary stasis, icteric necrosis of the liver cells occurs and fibrosis of a diffuse character may thus be favoured.

MORBID ANATOMY.

The liver in mechanical obstruction of the bile-ducts, though enlarged in the early stages, is small when seen at the autopsy, unless occupied by secondary growths or by a hydatid cyst. The surface is irregular, shows dilated and varicose bile-ducts filled with mucus, and is of a dark green colour. Occasionally there are perihepatitic adhesions. On section of the organ the dilated ducts are prominent objects and give the liver a sponge-like, honeycombed appearance, the substance of which is usually somewhat flabby from atrophy of the secreting cells, and cuts very differently from an ordinary cirrhotic liver. There is atrophy and condensation of the liver parenchyma around the dilated bile-ducts, and a certain amount of pericholangitic fibrosis. In cases where acute infection has been superadded there may be suppuration in or around the bile-ducts, and the formation of minute abscesses. The naked-eye appearances are therefore very different from those of hypertrophic biliary cirrhosis.

Further, the histological changes are not the same as those of hypertrophic biliary cirrhosis. In calculous obstruction the ducts are dilated and tend to become progressively more so in proportion to the duration of the obstruction, while in hypertrophic cirrhosis this does not occur. In biliary obstruction the larger ducts are chiefly affected and may show cholangitis and pericholangitis, while in hypertrophic biliary cirrhosis the smallest intra-hepatic ducts are inflamed. Rapid degeneration of the liver cells with focal necroses are marked features in mechanical obstruction of the larger ducts, whereas in hypertrophic biliary cirrhosis the liver cells maintain their nutrition for long periods. The small bile-ducts are not prominent; in one case Weber * found their number diminished.

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* Weber, F. P.: Trans. Path. Soc., vol. liv, p. 105.
† Compare Sharkey: St. Thomas Hospital Reports, vol. xviii, p. 245.
‡ Naunyn: Cholelithiasis, p. 163, Transl. New Sydenham Soc.

The columns of small cubical liver cells, known as "pseudobile canaliculi," are described in many cases, but are certainly not always present. Ford has laid stress on a wreathe-like arrangement of these pseudobile canaliculi. When fibrosis occurs it spreads out from the larger bile-ducts and may give rise to multilobular cirrhosis or to a more diffuse form of cirrhosis which not only tends to surround the individual lobules, but invades their substances and passes between the hepatic cells. From his study of 184 cases of cirrhosis, thought to be due to biliary obstruction, Mangelsdorf came to the conclusion that no particular form of cirrhosis could be said to depend on biliary obstruction.

The spleen is sometimes small or of normal size, but in cases where considerable fibrosis of the liver coëxists with obstruction of the larger ducts, as in Weber's † cases, there may be very considerable enlargement, though not to the same degree as in hypertrophic biliary cirrhosis.

The pancreas in cases where a calculus occupies the lower end of the bile-duct or the ampulla of Vater may, from obstruction combined with infection of its duct, show dilatation of the duct and fibrosis with atrophy of the ordinary secreting tissues of the organ. This chronic interstitial pancreatitis is perilobular and of a somewhat coarse form; only in very late stages does it become interacinous and lead to changes in the islands of Langerhans. As a rule, therefore, the islands of Langerhans, which provide the internal secretion of the pancreas, being preserved, diabetes mellitus is not produced.

CLINICAL FEATURES.

When cirrhosis of the liver, whether it be pericholangitic or portal, occurs in a patient with biliary obstruction, it does not, as a rule, reveal itself by any special signs or symptoms, the features being those of biliary obstruction. (*Vide* p. 532.) Complete aseptic obstruction of the common bile-duct leads to dilatation of the intra-hepatic ducts and to focal necrosis of the liver cells. The functional activity of the liver is thus very gravely interfered with, and as a result of this hepatic inadequacy, cholæmia or biliary toxæmia results, a condition which is much more rapidly fatal than cirrhosis. The symptoms are those of complete obstructive jaundice and cholæmia; the gall-bladder is usually dilated; this and the history should distinguish it from impacted gall-stone.

Cases of long-standing gall-stone obstruction of the common bile-duct associated with ordinary portal cirrhosis undoubtedly occur. As a rule, symptoms of portal cirrhosis are absent or cast into the shade by those of biliary obstruction. But in some instances the manifestations of cirrhosis, such as ascites and dilated veins over the abdomen, are present.

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* Weber: Trans. Path. Soc., vol. liv, p. 110.

† Weber, F. P.: Trans. Path. Soc., vol. liv, p. 118.

In some instances the clinical features of ordinary portal cirrhosis may develop after obstruction due to gall-stones or other causes has been established; the cirrhosis is then reasonably explained as the result of poisons manufactured in the intestines and carried to the liver by the portal vein.

Ford has collected 10 cases in which ascites and other symptoms of portal cirrhosis were associated with obstruction of the common bile-duct. In six of these the obstruction was by gall-stones, and in four by tumors, glands, or a cicatrix pressing on the duct from without.

Finally, biliary obstruction does not give rise to any fixed type, either pathological or clinical, of cirrhosis.

In instances where a gall-stone becomes lodged in the common bile-duct without any history of colic being obtained the question of diagnosis may be one of considerable difficulty. As time progresses bile may escape by the side of the stone into the duodenum and the fæces are no longer pale; they then contain bile, just as they do in hypertrophic biliary cirrhosis. In differentiating these two conditions, the size of the spleen is important; it is much enlarged in hypertrophic biliary cirrhosis, while in gall-stone obstruction the spleen, if at all increased in size, is relatively insignificant. In hypertrophic biliary cirrhosis the liver is greatly increased in size; in biliary obstruction it may be swollen from retention of bile, but in the late stages it becomes smaller.

TREATMENT.

The treatment is that of obstructive jaundice by operative measures and by symptomatic remedies. (*Vide* p. 555.) In the rare cases where there are ascites and symptoms pointing to ordinary cirrhosis the treatment should be on the lines of that disease.

HEPATIC CIRRHOSIS IN CHILDREN.

Cirrhosis is far from common in children, though probably not quite so rare as might be concluded from the late Dr. C. West's * experience of only 4 examples of cirrhosis in 70,000 cases of children's diseases. In 1889 Hatfield † was able to refer to 156 cases of cirrhosis in children. Since then a very considerable number are to be found, scattered about in medical literature, as shown by the fact that in 1899 Musser ‡ collected 529 additional cases. Children are affected by the forms of cirrhosis seen in adults, and in the main react in very much the same manner. In the following summary dealing with cirrhosis in children reference will only be made to points deserving special attention.

The various forms of cirrhosis of the liver that occur in children have a distinct tendency to attack more than one member of the family; this depends on hereditary influences, of which syphilis is preëminent, and on the fact that exposure to influences favouring cirrhosis, such as alcohol and improper food, etc., form part of the family environment.

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* West, C.: Lectures on Diseases of Infancy and Childhood, p. 654, 1884.

† Hatfield: Cyclopædia of Children's Diseases, vol. iii, p. 488.

‡ Musser, J. H.: Supplement to Cyclopædia of Children's Diseases, 1899, p. 798.

The pericellular cirrhosis of hereditary syphilis and the lesions of tardive hereditary syphilis will be fully dealt with elsewhere (p. 375), and it will then be pointed out that after recovery from pericellular cirrhosis the liver is probably left with its resistance so diminished that it may readily become affected by ordinary portal cirrhosis, the resulting change being neither due to syphilis nor curable by anti-syphilitic treatment, but disposed to by the influence of former syphilis, and therefore parasyphilitic and comparable to locomotor ataxia and general paralysis of the insane. Some cases of marked portal cirrhosis in early life may thus be distantly related, though not directly due to syphilis.

There are other forms of intra-uterine or *congenital cirrhosis*. It occurs in a marked form in congenital obliteration of the bile-ducts, and is seen in cases which clinically resemble that group, but anatomically do not present obliteration of the ducts. It is reasonable to believe that the change is due to poisons conveyed from the mother to the fœtus. For a discussion on this point the reader is referred to the section on Congenital Obliteration of the Bile-ducts.

Vanverts and Ramond * record an interesting case of congenital ascites and hepatic cirrhosis in which the fœtus' abdomen had to be tapped before it could be delivered. The liver was enlarged and cirrhotic. There was no evidence of syphilis, alcoholism, or tuberculosis in the parents.

Portal Cirrhosis.—As in adults, the liver may be larger than normal, or may be small and markedly hobnailed. In cases where nodular hyperplasia is well marked the liver may look as if occupied by multiple new-growth. In some cases the cirrhosis can be traced to precocious alcoholism, or to some specially irritating kind of food, such as fish, etc., soaked in vinegar. It is, therefore, not surprising that occasionally two or more children in the same family suffer from portal cirrhosis. (*Vide* p. 181.) In many cases alcoholism can be excluded and some other cause must be sought for, such as gastro-enteritis or the specific fevers. Probably some of the cirrhotic livers of early life are, like granular kidneys in childhood, in reality parasyphilitic; it is interesting in this connexion to note that cirrhosis has been observed in juvenile general paralysis of the insane due to hereditary syphilis.

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Wilks: Trans. Path. Soc., vol. xiv, p. 175.

Clinical Features of Portal Cirrhosis in the Young.—Hæmatemesis seems less frequent than in adults, possibly because the spleen is more distensible and therefore accommodates relatively more portal blood than in the adult. Saunal,* however, records a case of fatal hæmorrhage from an œsophageal varix in a girl aged twelve years. Hæmorrhages elsewhere, from the nose and into the skin, and depending on severe toxæmia, are quite as frequent proportionately as in adults. The enlargement of the liver and spleen is more prominent than in adults. This may in part depend on the liver being relatively larger in children and on greater power of repair and hyperplasia of the liver in early life. The spleen is more readily distended in early life. In children mixed cases of portal and biliary cirrhosis are not infrequent; this, again, bears on the more marked enlargement of the liver and spleen.

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* Vanverts and Ramond: Bull. Soc. Anat. Paris, 1896, p. 153.

A raised temperature is more frequent in children than in adults. The fever may be so marked as to suggest typhoid fever or generalised tuberculosis.

In a case of Dr. Wickham Legg's † a boy aged twelve years was first thought to have typhoid fever and later acute tuberculosis. Another case regarded as typhoid fever occurred at St. George's Hospital. (*Vide* p. 219.)

Ascites is not uncommon, and is very likely to be regarded as evidence of tuberculous peritonitis. Pulmonary tuberculosis is very rarely seen as a complication, but infection of the peritoneum may occur. In some cases a terminal suppurative peritonitis is met with. A curious symptom sometimes observed is ravenous appetite. Jaundice, often quite slight, and diarrhœa are more often found in association with cirrhosis in children than in adults.

In an interesting group of cases described by Ormerod ‡ and Homén § the symptoms are entirely nervous and cirrhosis is not suspected during life. These cases show loss of power, muscular contractures, mental weakness progressing to idiocy, fever, and great emaciation. The condition may occur in several members of the same family. (Gowers, ‖ Homén.) Cirrhosis of the liver and inflammatory softening in the lenticular nuclei are found after death. Homén regarded his cases as due to hereditary syphilis, and it is quite conceivable that they were examples of juvenile general paralysis of the insane in which parasyphilitic cirrhosis of the liver was also present.

Hypertrophic biliary cirrhosis is relatively a commoner form of cirrhosis in children than in adults; it presents some special features which Gilbert and Fournier ** have described as the juvenile type of the disease. Development is arrested and the condition termed "infantilism" results. The cases may run an extremely protracted course, and the type of the disease may change, and eventually present the features of ordinary or portal cirrhosis. The latter morbid condition supervenes in biliary cirrhosis just in the same way that interstitial fibrosis may occur in protracted cases of chronic parenchymatous nephritis and lead to a contracting white kidney with a corresponding change in the clinical aspect of the case. For the account of the disease the reader is referred to page 306.

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* Saunal: Thèse Paris, 1892.
† Legg, Wickham: St. Bartholomew's Hospital Reports, vol. xiii, p. 148, 1877.
‡ Ormerod, J. A.: St. Bartholomew's Hospital Reports, vol. xxvi, p. 57, 1890.
§ Homén: Neurologisches Centralblatt, S. 514, 1890. Quoted by Ormerod.
‖ Gowers: Diseases of Nervous System, vol. ii, p. 656, 1886.
** Gilbert and Fournier: Soc. de biolog., 1895, 419.

Cirrhosis in Young Children in India.—A peculiar form of cirrhosis among young native children in India, attacking chiefly Hindus, has been described by Gibbons,[*] Ghose,[†] and others.[‡] It occurs especially around Calcutta, but is by no means limited to that part of India. It is common—Ghose had seen as many as 400 cases personally—and extremely fatal, often killing off one child after another in the same family; about 95 per cent. of those attacked die from the disease before the end of the second year of life. In 1891–93 there were 1748 deaths in Calcutta; only six of Ghose's 400 cases recovered. It is not due to syphilis, alcohol, or malaria. It has been thought to depend on irritating bodies in the food (*vide* Etiology, p. 187). The change begins as a pericellular cirrhosis, and then becomes interlobular; the amount of fibrous tissue may be very large, there is great destruction of the liver cells, and extensive formation of new bile-ducts. Kundrat and Paltauf of Vienna, to whom Gibbons showed his specimens, regarded the change as a hitherto undescribed form of biliary cirrhosis. The spleen is usually enlarged. The disease is not congenital, but generally begins about seven months of age with fever and enlargement of the liver and spleen. There is constipation, nausea, and jaundice which eventually becomes intense. A terminal ascites may develop.

In rickets the liver is enlarged, in addition to being somewhat displaced downwards by deformity of the chest. As the result of absorption of toxic products from the alimentary canal there is some fatty change in the liver cells and fibrous hyperplasia in the portal spaces.[§] Hogben [‖] seems alone in describing the change as a biliary cirrhosis. The change seems to be temporary and of no importance; it does not appear to be the precursor or first stage of cirrhosis. The changes in the liver secondary to morbus cordis and spoken of as cardiac cirrhosis, pericarditic hepatic pseudo-cirrhosis, and cardiotuberculous cirrhosis (*vide* p. 101) are chiefly met with in children.

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[*] Gibbons, J. B.: Scientific Memoirs by Medical Officers of the Army of India, part vi, 1891, and the Indian Lancet, May 1, 1896, p. 426.

[†] Ghose: Lancet, 1895, vol. i, p. 321.

[‡] Nil Ratan Sircar: Indian Lancet, July 1, 1896. Mackenzie: Lancet, 1895, vol. i.

[§] *Vide* W. H. Dickinson: Enlargement of the Viscera in Rickets, Trans. Royal Medical and Chirurg. Soc., 1869.

[‖] Hogben: Birmingham Med. Review, vol. xxiv, p. 65, 1888.

TUBERCULOSIS OF THE LIVER AND BILE-DUCTS.

SYNOPSIS.

- *Introduction.*
- *Paths by which tubercle bacilli reach the liver.*
  - By the umbilical vein (congenital tuberculosis); hepatic artery; portal vein; lymphatics; bile-duct.
- *Forms of hepatic tuberculosis.*
  - (I) Miliary tuberculosis.
  - (II) Local tuberculosis.
    - (*a*) Involving the bile-ducts.
    - (*b*) Solitary tubercle. Abscess.
- *Other changes in the liver* associated with tuberculosis.
  - Focal necrosis. Fatty, lardaceous change.
  - Tuberculosis and cirrhosis.

INTRODUCTION.

Tuberculosis of the liver has little clinical importance, can seldom be diagnosed with certainty during life, and when found after death is usually part of generalised tuberculosis. Larger tuberculous masses are more often seen in children and young subjects than in adults, but seldom give rise to clinical manifestations. In the exceptional instances where a tuberculous mass or abscess has produced enlargement of the liver, some commoner result of tuberculosis, such as fatty or lardaceous change, would probably be diagnosed. The comparative infrequency of advanced tuberculous changes in the liver might suggest that, like the thyroid gland, the liver is inimical to the growth of the tubercle bacillus. This is probably not the case, for in lower animals, especially in birds, hepatic tuberculosis is common, and Sergent * has shown experimentally that the bile is not more antagonistic to the growth of tubercle bacilli than of other micro-organisms. It is probable that the reason why advanced tuberculous changes are rare in the liver is that the liver does not, like the mesenteric glands, lie in the direct line of the lymphatic vessels conveying lymph from the intestines. The lymphatic glands in the portal fissure receive the efferent lymphatic vessels conveying lymph away from the liver. In order that tuberculous infection should pass into the liver along the lymphatics of the portal fissure the bacilli would have to work their way against the flow of lymph. Possibly this does occur, but in most cases where the intestines, the liver, and the lymphatic glands in the portal fissure are tuberculous, the tubercle bacilli have probably travelled from the intestine to the liver by the portal vein, set up tuberculous foci in the portal canals, and so infected the lymphatic glands in the portal fissure.

Marmorek,† however, finds from experiment that there is a certain amount of immunity to tuberculous infection on the part of the liver which cannot be satisfactorily explained on the anatomical grounds mentioned above. He believes that chemical factors inhibit the development of tubercle bacilli in the liver.

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* Sergent: Thèse Paris, 1895–6, No. 92.

† Archiv. Général. de Méd., Nov. 24, 1903.

PATHS BY WHICH TUBERCLE BACILLI CAN REACH THE LIVER.

Tubercle bacilli may reach the liver from various sources.

By the Umbilical Vein.—During fœtal life, if there were tuberculous disease of the placenta the bacilli would reach the liver by the umbilical vein. This is so very rare and exceptional that it can only be regarded as a pathological curiosity. It is chiefly interesting from Baumgarten's theory that tubercle bacilli are retained in the liver from early fœtal life in the form of spores. Experimentally tuberculosis of the liver in the fœtus has followed local tuberculous infection of the genital organs in guinea-pigs. (D'Arrigo.[*]) Cases of hepatic tuberculosis in children within the first fortnight of life have been described by Sabouraud [†] and by Horl, and are undoubtedly due to infection during fœtal life. Fœtal tuberculosis in calves appears to be equally rare, but its existence has been established by Nocard,[‡] MacFadyean,[§] and Johne.

By the Hepatic Artery.—In generalised tuberculosis tubercle bacilli reach the liver by the hepatic artery. It is probable that tubercle bacilli often reach the liver when, although a number of bacilli have gained entrance to the general circulation, generalised tuberculosis does not result. Thus, in chronic pulmonary tuberculosis tubercles in the liver may be due to bacilli which have strayed into the blood-stream. The miliary tubercles are scattered through the liver both inside the lobules and in the portal spaces. It is possible that when a number of tubercles thus arise in the portal spaces they may increase in size and form a caseous mass which bursts into the bile-ducts and thus gives rise to the condition described as tuberculous cholangitis. But death usually occurs from tuberculous lesions elsewhere, *e. g.*, meningitis, long before this sequence of events can complete itself in generalised tuberculosis, and it is only exceptionally that tuberculous cholangitis or abscess is due to bacilli reaching the liver by the arterial blood.

By the Portal Vein.—Tubercle bacilli from the bowel in cases of tuberculous ulceration readily pass by the portal vein to the liver, and there set up either miliary tubercles, or the larger and more chronic tuberculous changes in connexion with the bile-ducts. Tubercle bacilli can pass through the mucous membrane of the intestine without any gross lesion of the mucous membrane. Sergent[‖] insists that tubercle bacilli first set up inflammation and thrombosis of the terminal intrahepatic branches of the portal vein before tuberculous changes occur in the immediate neighbourhood of the bile-ducts, but I have not been able to convince myself of this.

By the Lymphatics.—In cases of tuberculous peritonitis bacilli may possibly work their way in through the lymphatic vessels of the capsule and gain a footing in the substance of the liver, but as a matter of fact there is very little evidence that hepatic tuberculosis is set up in this manner. It is also conceivable that from tuberculosis of the glands in the portal fissure, secondary to intestinal disease, an extension of the disease to the inside of the liver may result. But, as already pointed out, this spread of tuberculosis is against the current of lymph, the lymphatics at the portal fissure running away from, not towards, the liver.

By the Common Bile-duct.—It has been suggested that tubercle bacilli from the duodenum pass up the bile-ducts, work their way through the mucous membrane of the ducts into the portal spaces, and there give rise to the formation of caseous tubercles. This view, which on the face of it was improbable from the absence of motility on the part of the tubercle bacilli, has been disproved by Sergent's experiments of injecting tubercle bacilli into the bile-ducts, which showed that unless the walls of the ducts were previously damaged, as by ligature, they did not allow tubercle bacilli to pass through them. It is noticeable that the extra-hepatic ducts are not affected by tubercle except in the rarest instances, and that there is no condition of ascending or descending tuberculous cholangitis to correspond with tuberculous disease of the ureter. Pilliet [**] suggested that tubercle bacilli might be excreted from the blood into the lumen of the ducts and that tuberculous cholangitis then results. Microscopic examination, however, of such cases, viz., where the ducts are involved (*vide* p. 342) shows that the tuberculous process always begins outside the ducts.

To sum up: Tubercle bacilli reach the liver by the hepatic artery in generalised tuberculosis and in conditions which fall short of generalised tuberculosis. The portal vein also conveys tubercle bacilli to the liver, but there is no evidence that tubercle bacilli travel up the bile-duct and very little to show that hepatic tuberculosis is conveyed through the lymphatics.

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[*] D'Arrigo: Centralbl. f. Bakt., 1900.

[†] Sabouraud: Soc. de biolog., 1891, p. 674.

[‡] Nocard: Rev. de la Tuberculose, 1895.

[§] MacFadyean, J.: Trans. Path. Soc., vol. l, p. 268.

[‖] Sergent, E.: Thèse Paris, 1895.

[**] Pilliet: Thèse Paris, 1891.

FORMS OF HEPATIC TUBERCULOSIS.

It might be thought more methodical to consider hepatic tuberculosis under two heads—(i) tuberculous disease of the liver substance proper and (ii) tuberculosis of the bile-ducts. But since, as will be shown later, the ducts themselves are not affected primarily and only suffer as the result of extension from without, whether the starting-point is in the liver substance, the portal space, or in exceptional instances the lymphatic glands in the hilum, it is more practical to divide the subject of hepatic tuberculosis into—

(I) Miliary tuberculosis,—(*a*) part of acute generalised tuberculosis; (*b*) due to infection from the intestine.

(II) Local tuberculosis—(*a*) involving the ducts; (*b*) not involving the ducts.

MILIARY TUBERCULOSIS.

The presence of miliary tubercles in the liver is part of generalised tuberculosis, and though sometimes not seen on naked-eye examination, they will be found to be constantly present when microscopic sections of the liver are made. Miliary tubercles are found in the liver in chronic pulmonary tuberculosis as a result of two processes: (*a*) tubercle bacilli reaching the liver by the hepatic artery, and (*b*) tubercle bacilli derived from secondary tuberculous ulcers in the intestine and passing to the liver by the portal vein.

Simmonds * found hepatic tubercles in 82 per cent. of 476 cases of tuberculosis, 76 per cent. in adults, 92 per cent. in children. Zehden † found miliary tubercles in 50 per cent. of all fatal cases of pulmonary tuberculosis, thus corresponding with the frequency of tuberculous ulceration of the intestine in that disease. My own experience would put the occurrence of miliary hepatic tubercle in fatal cases of ordinary pulmonary tuberculosis lower than 50 per cent.

Miliary tubercle in babies at birth is almost a pathological curiosity. When there is tuberculosis of the placenta the bacilli may infect the liver by the channel of the umbilical vein. Bar and Renon ‡ have found tubercle bacilli in the blood of the umbilical vein of two fœtuses from mothers affected with tuberculosis. Sabouraud § met with miliary tubercles in the liver and spleen of a newly born infant eleven days old whose mother had pulmonary tuberculosis.

Morbid Anatomy.—Miliary tubercles in the liver are small and isolated, grey, and when older yellow in colour, and are better seen on the surface of the capsule than on section of the organ. In some instances the liver may be crowded with minute miliary tubercles which can only be seen when microscopic sections are made; to the naked eye the liver may merely show cloudy swelling. In the substance of the liver the tubercles are nearly always situated inside the lobules and thus form a contrast to the local and chronic form of tuberculosis of the liver occupying the portal spaces. Miliary tubercles are not infrequently found in cirrhosis of the liver and are then usually a superadded lesion and not the cause of the cirrhosis. The liver is generally fatty and rather increased in weight; there may be considerable venous engorgement from terminal failure of the right side of the heart. Usually there is little or no tuberculous perihepatitis, but this may coëxist with miliary tubercles in the substance of the liver under two conditions: (I) When there is chronic peritonitis of tuberculous origin in which the capsule of the liver shares, or (II) in rare instances where there is a subacute fibrinous peritonitis associated with acute miliary tuberculosis of the capsule of the liver. It is possible that the miliary tubercles in the hepatic substance may, if the process is not very acute in its generalisation, have time to unite and form small caseous areas which may soften down and form small tuberculous abscesses.

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* Simmonds: Centralblatt f. Path., 1898, Bd. ix, S. 865.
† Zehden: Centralblatt f. Path., 1897, Bd. viii, S. 468.
‡ Bar et Renon: Soc. de biolog., June 29, 1895, p. 505.
§ Sabouraud: Soc. de biolog., Oct. 17, 1891, p. 674.

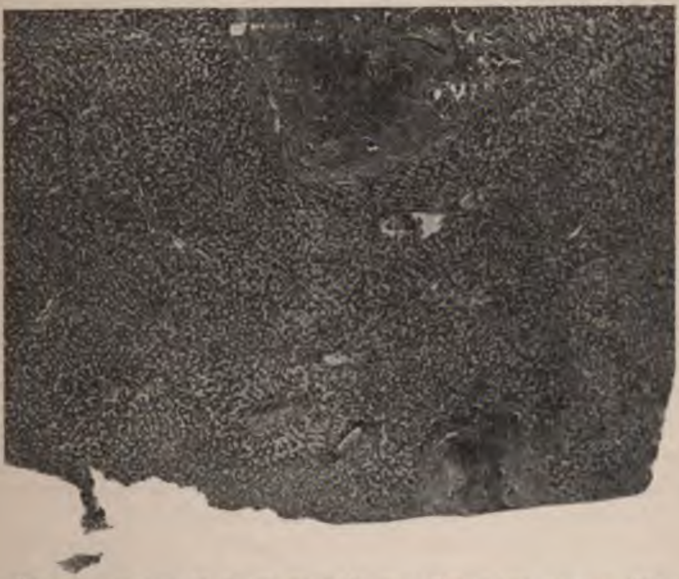

FIG. 40.—PHOTOMICROGRAPH OF LIVER WITH CASEOUS TUBERCLES SHOWING GIANT CELLS. The liver substance shows chronic venous engorgement. (S. G. Penny, Esq.)

In a child aged three months who died in St. George's Hospital with advanced tuberculous bronchopneumonia the liver contained a large number of miliary tubercles and two tuberculous cavities stained with bile, rather larger than a pea. The intestines were free from tuberculosis. Sergent has described a unique case of confluent miliary tuberculosis of the liver.

Histology.—In their earliest stage tubercles consist of small round cells, like masses of lymphoid tissue, with a delicate reticulum. McWeeney * considers that many of the tubercles begin by proliferation of the endothelium of the interlobular capillaries. After a time larger endothelioid cells are found in the miliary tubercle; they are the result of inhibited hyperplasia of the cells which at first were small. When the tubercle grows to a larger size, according to McWeeney, 0.2 mm., giant cells appear. The giant cells are due to union of preëxisting cells, though it has been thought that continued growth and nuclear division without cellular division in endothelioid cells might account for them. The central part of the giant cells becomes homogeneous and caseous, while the nuclei form prominent objects around the periphery. It is often impossible to demonstrate bacilli in perfectly typical tubercles. The liver cells at the margin of the tubercles are compressed and may undergo fatty change. In some cases the fatty change is widely diffused throughout the liver.

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* McWeeney: Brit. Med. Journ., 1900, vol. i, p. 844.

Signs and Symptoms.—There are *no clinical signs or symptoms* which can be relied upon to indicate the presence of miliary tubercles in the liver. Hilton Fagge * and Fränkel † have seen it associated with jaundice, but this is so rare as to be practically a curiosity. When there are a large number of tubercles on the surface of the liver, it is possible that a friction rub may be heard on auscultation.

LOCAL TUBERCULOSIS.

(I) Involving the bile-ducts.
(II) Solitary tubercle of the liver. Tuberculous abscess.

Tuberculous Disease Involving the Bile-ducts.

Synonyms: Tuberculous Cavities in the Liver. Tuberculous Cholangitis or Pericholangitis.

Incidence and Etiology.—Though this condition was described by Bristowe ‡ in 1858, who found it present in 12 out of 167 cases of tuberculous ulceration of the intestines, it has not attracted much general attention, probably because it has no clinical features. It is a commoner condition than the number of recorded cases would lead one to suppose. The tubercle bacilli reach the liver by the portal vein, being derived from the intestines, which in most instances show tuberculous ulceration. Tubercle bacilli having reached the liver settle down in the portal spaces and produce miliary tubercles, and later masses of tuberculous granulation tissue. The condition might well be spoken of as tuberculosis of the portal spaces.

Sergent § insists that the first step is tuberculous pylephlebitis and thrombosis of the intra-hepatic branches of the portal vein, and that at a later stage tuberculous granulation tissue develops in the portal spaces.

The tuberculous granulation tissue caseates, softens down, and eventually breaks into the bile-ducts from without inwards. The discharge of the tuberculous foci into the ducts is analogous to rupture of a caseous focus in the lung into the bronchi. The ducts become infected and may

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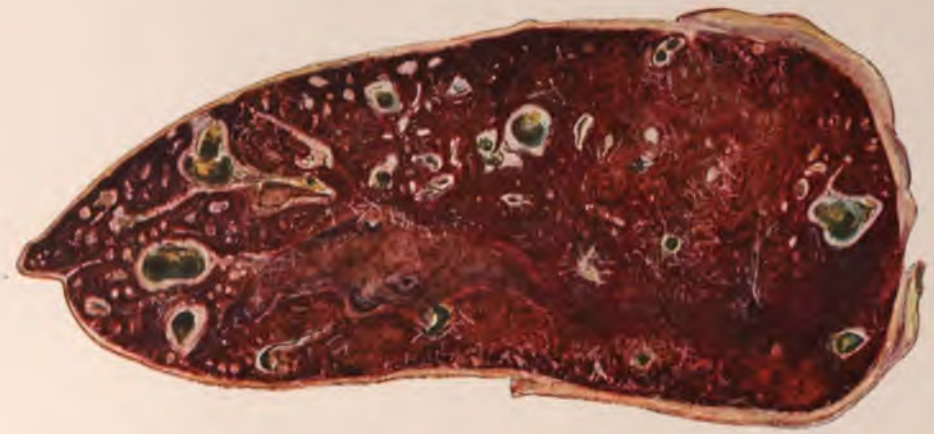
* Hilton Fagge: Text-book of Med., vol. ii, p. 270, 1886.
† Fränkel, A.: Zeitschrift f. klin. Med., Bd. v, S. 107, 1882.
‡ Bristowe, J. S.: Trans. Path. Soc., vol. ix, p. 241.
§ Sergent; Thèse Paris, 1895, No. 92.

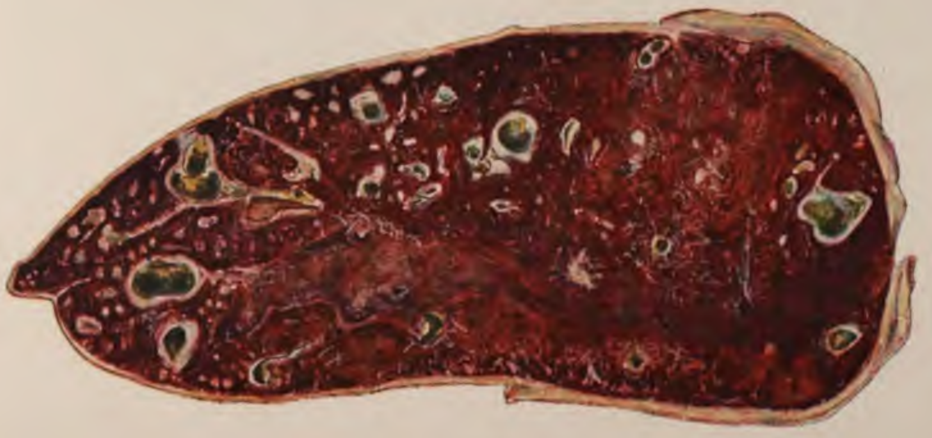
PLATE 3.



SECTION OF LIVER SHOWING TUBERCULOUS CAVITIES IN PORTAL SPACES, COMMUNICATING WITH THE BILE-DUCTS AND STAINED GREEN WITH BILE.

From a case recorded by Dr. C. Dudgeon. Painted by L. Jones, M. B., F. R. C. S.

PLATE 3.



Section of Liver Showing Tuberculous Cavities in Portal Spaces, Communicating with the Bile-ducts and Stained Green with Bile.

From a case recorded by Dr. C. Dudgeon. Painted by L. Jones, M. B., F. R. C. S.

be entirely destroyed locally. The communication between the cavities thus formed and the ducts is not always visible, but from the bile-stained condition of the "vomicæ" there can be no doubt this has occurred. (Compare Wethered's case.*)

As stress has been laid on the statement that the bile-ducts are invaded from without or are secondarily involved in tuberculous disease of the liver, it ought to be mentioned that Lancereaux † has described a case of tuberculosis of the common bile-duct, gall-bladder, and cystic duct in a woman aged thirty-two years, which he regards as directly due to infection from the duodenum.

Morbid Appearance.—The liver is usually somewhat larger than natural, and on section shows a number of white caseous areas or of bile-stained cavities with caseous walls. In the earlier stages, before the tubercles have opened into the ducts, the tuberculous material is firm and resembles, and is therefore sometimes regarded as, lymphadenoma; in the later (excavation) stage, when they have opened into a bile-duct, their walls have a greenish-yellow colour from bile-staining, and exceptionally a purple colour from hæmorrhage. In their early stage the tubercles may be ⅙ to ¼ inch in diameter, while the cavities subsequently developed are larger and may measure as much as an inch or even two inches across.

Structurally the masses are enclosed in a capsule representing the fibrous tissue of the portal space, and contain caseating granulation tissue surrounding a cavity which in its turn can be seen opening into a bile-duct; the epithelium of the bile-duct may be well preserved except at the point where it has been destroyed by the perforation from without. The tuberculous process is therefore primarily pericholangitic not cholangitic. Further, the bile-duct is not affected throughout its course in the way that a tuberculous ureter is, but is locally infected at the spot where it is invaded from without. The larger extra-hepatic ducts are very seldom involved; a softened tuberculous gland in the hilum of the liver may exceptionally open into the bile-duct.

Kester ‡ has recorded a case which would bear this interpretation. A boy aged three years had jaundice, due to pressure of tuberculous portal glands, and tuberculous pneumonia. The liver contained tubercles and the ducts were dilated and the lower end of the common bile-duct opened into a caseous cavity.

Macroscopic Diagnosis.—Tuberculous masses and cavities in the liver sometimes closely resemble other conditions. The deep bile-staining is extremely suggestive of tuberculous cavities in connexion with the bile-ducts, but before this staining has occurred the masses may resemble nodules of lymphadenoma, etc. The tuberculous masses are whiter and may show signs of breaking down, which lymphadenoma never does. In cirrhosis with multiple adenomata fatty change in the nodular areas of hyperplasia has often given rise to a mistaken diagnosis of tuberculous masses. In exceptional instances secondary carcinoma may very closely imitate tuberculous masses and necessitate microscopic examination. The rare condition, chronic pericholangitis, of which Strangeways Pigg and I,§ and Morley Fletcher ‖ have recorded examples, exactly imitates tuberculous cavities in the liver. Psorospermial disease of the bile-ducts in tame rabbits closely imitates tuberculous lesions, and though it is extremely rare in man, it is conceivable that some examples of this protozoan infection have been erroneously called tuberculous. Actinomycosis and the suppurating foci in pylephlebitis and cholangitis are hardly likely to be mistaken for tuberculous cavities, though abscesses at first regarded as tuberculous have been subsequently shown to be actinomycotic.*

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* Wethered, F. J.: Trans. Path. Soc., vol. xl, p. 139.

† Lancereaux: Traité des Maladies des Foie et du Pancreas, p. 662, 1899.

‡ Kester: Centralblatt f. inn. Med., 1896, S. 213.

§ Rolleston and Strangeways Pigg: Journ. of Pathology and Bacteriology, vol. v, p. 221, 1898.

‖ Morley Fletcher: Trans. Path. Soc., vol. lii, p. 193.

Histologically the portal space is occupied by tuberculous granulation tissue containing giant cells and undergoing caseation. This surrounds the bile-duct and opens into it. Eventually the bile-duct may be destroyed, and at this stage the portal space contains a central mass of caseous débris, stained with bile, and surrounded by tuberculous granulation tissue.

Clinical Features.—There are very seldom any definite symptoms pointing to the liver. It is indeed remarkable that jaundice is constantly absent, inasmuch as there is very definite obstruction in, at any rate some of, the bile-ducts.

It seems possible that the reason why jaundice is not met with is that the lymphatic vessels which should carry the bile from the obstructed ducts are themselves compressed and are unable to convey the bile into the general circulation. If this be the case, the liver substance should be bile-stained. Since this does not occur in cases of tuberculous cavities in the liver, this explanation cannot be urged.

It is true that occasionally attacks of abdominal pain have been reported in cases where tuberculous cholangitis was found after death. These attacks of pain are not accompanied by jaundice or by bile in the urine and are not likely to suggest biliary colic during life. The abdominal pain is very probably due to tuberculous ulceration of the intestines or concomitant tuberculous peritonitis. Ascites may result from tuberculous peritonitis, or conceivably from compression of the portal vein by enlarged tuberculous glands. As a rule, the clinical aspect of the cases presenting this condition after death are those of pulmonary, abdominal, or generalised tuberculosis.

I examined after death a child aged nine months who had advanced tuberculous disease of the lungs, tuberculous ulcers in the intestine, caseous mesenteric glands, and tuberculous cavities in the liver. During life the signs were those of consolidation of the lungs; there was no diarrhœa or jaundice. Dudgeon showed a good specimen of tuberculous cavities in the liver to the Pathological Society from a girl aged two years; there were tuberculous ulcers in the intestine, tuberculous peritonitis, and adenitis of the lymphatic glands in the portal fissure. Plate 3 is taken from a section of the liver presented by Dr. Dudgeon to the museum of St. George's Hospital.

Solitary Tubercle.

Under the heading of "solitary tubercle" it will be convenient to consider comparatively large masses of caseous material which do not communicate with the bile-ducts. It is true that such masses might soften down and effect a fistulous communication with the bile-ducts, but it would then be impossible to be certain that the tuberculous process had not started near the bile-ducts. Although called "solitary tubercle," there may be a number of these caseous masses in the liver. This form of local tuberculosis, in which the portal spaces and bile-ducts are not specially involved, is rare, but is common in some animals.

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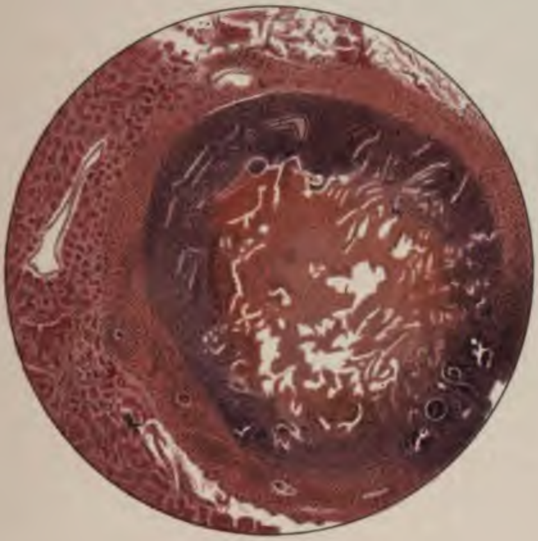
* Harley, J.: Medico-Chirurg. Trans., vol. lxix, p. 135, 1886. Shattock, S. G.: Trans. Path. Soc., vol. xxxvi, p. 260.

PLATE 4.



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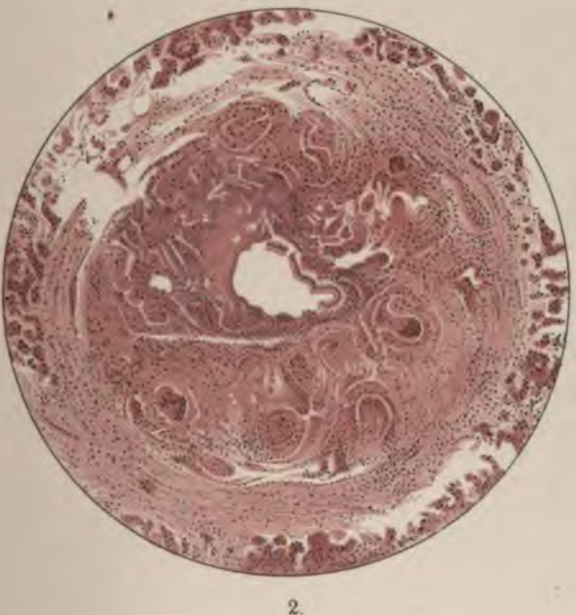

2.

1. ADVANCED STAGE OF A TUBERCULOUS CAVITY IN THE LIVER.

There is a dense fibrous capsule derived from the portal space which surrounds tuberculous granulation-tissue; more internally there is a mass of caseous debris.

2. Earlier stage, showing tuberculous granulation tissue occupying the portal space and opening into the bile-duct.

Masses of hard caseous tubercle are very common in birds; in fact, the liver is the chief, and in 20 per cent. of the cases examined by W. Hutchinson * the only, organ affected in avian tuberculosis. In bovines large caseous masses are found in the liver; they soften from suppuration and have a thick fibrous capsule.

These solitary caseous masses are rather less rare in children than in adults.

Craven Moore,† who reports a case, only refers to four other published instances, by Clement, Zehden, and Simmonds two. I think, however, they are not nearly so rare as this, and have certainly seen two. F. Craven Moore's case was extremely interesting in that there were 8 tuberculous masses in the liver of a man who died with carcinoma of the pylorus. It was thought that the tubercle bacilli were absorbed from the ulcerated surface in the stomach and that the absence of HCl in the gastric juice rendered this infection more feasible. Clement ‡ has described an almost exactly similar case. Inasmuch as tubercle bacilli were not found in either Moore's or Clement's cases, the possibility arises that there may have been some other cause for the caseous masses, such as the pseudo-tuberculosis bacillus described by A. Pfeiffer and by Klein. Klein § found a bacillus in Thames and Lee water and produced caseous masses by means of it in the liver, lung, and lymphatic glands. It is possible that in cases of carcinoma of the stomach these bacilli introduced into the stomach in water might set up caseous lesions in the liver.

The following is a well-marked example of multiple "solitary" tuberculous masses in the liver:

A boy aged eight years was under my care in St. George's Hospital for the greater part of thirteen months; he was admitted with pericarditis and advanced renal disease; he recovered from the pericarditis and gradually developed multiple tuberculous lesions of the limbs, skull, and vertebræ. It was noticeable that as the tuberculous lesions advanced his renal symptoms receded. There was never any jaundice. He eventually died of exhaustion. The liver was much enlarged as compared with his emaciated body; weight, 20 ounces. There was tuberculous perihepatitis with large white caseous masses, unstained with bile, in the liver. They were the size of filbert nuts and had been felt during life projecting from the surface of the liver. No communication with the bile-ducts could be made out; the mesenteric, tracheal, inguinal, and axillary glands were also tuberculous.

Milian and Hertz ‖ have recorded the case of a man aged fifty-eight with emaciation, an enlarged spleen, and fever unaffected by quinine. The clinical aspect suggested malaria or tuberculosis, but no signs were found in the lungs. The liver contained miliary tubercles and larger ones as big as a horse-chestnut; the spleen was also affected; but there were no tubercles in the alimentary canal or lungs. In a somewhat similar case—a woman aged sixty-six years—described by Tolot ** there were no intestinal or pulmonary lesions.

Around the white caseous masses there is a thin fibrous capsule, while outside this the liver substance is compressed and the cells elongated and flattened. The caseous masses may be fairly easily enucleated. These "solitary" tubercles closely resemble gummata, and must be distinguished from the appearance presented by the adenomatous formations in nodular hyperplasia when fatty degeneration has occurred in the hyperplastic liver cells. In a few instances encysted caseous masses have also been found in the spleen. (Milian and Hertz; Tolot.)

The clinical aspect, as has been shown incidentally by the foregoing cases, is vague and in no way characteristic. The liver may not be made out to be enlarged. Exceptionally a tuberculous mass may be sufficiently large to be felt through the abdominal walls during life.

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* Woods Hutchinson: Studies in Human and Comparative Pathology, p. 304.

† Craven Moore: Medical Chronicle, Oct., 1899, p. 5.

‡ Clement: Virchow's Archiv, Bd. cxxxix, S. 35.

§ Klein, E. E.: Lancet, 1899, vol. ii, p. 1297.

‖ Milian and Hertz: Bull. Soc. Anat. Paris, 1900, p. 153.

** Tolot: Lyon Médical, vol. xcix, p. 323, Sept. 7, 1902.

Thus, in a case related by T. L. Anderson * a mass the size of a Mandarin orange in the left lobe of the liver was distinctly felt during life. The patient was a man aged forty-one who had extensive intestinal tuberculosis.

In a few cases the spleen is palpably enlarged. Jaundice does not occur, and a diagnosis can hardly be made. As a rule, the patients suffer from increasing weakness, loss of appetite, and general debility.

Excision of a tubercular mass has been carried out by Rome † and Ransohoff,‡ in the first case with recovery.

Tuberculous Abscess.—The solitary tubercles may become secondarily infected with pyogenetic micro-organisms, soften down, and form abscesses; this occurred in H. Mackenzie's § case, where the cavities were purple and contained blood but not bile. In rare instances tuberculous abscesses may reach a considerable size; they may set up local perihepatitis or even perforate into the peritoneal cavity. Waring,‖ from a surgical point of view, considers tuberculous abscess of the liver as being either entirely inside the liver, and so resembling an ordinary hepatic abscess, or when near the surface of the organ setting up a localised perihepatic abscess which may then resemble and indeed be a subphrenic abscess.

A single tuberculous abscess of the liver is very rare indeed. Some of the cases that have not been examined microscopically may have been softened gummata or actinomycotic abscesses. (*Vide* p. 342.)

Mayo Robson ** operated upon an hepatic abscess which proved to be tuberculous and was evidently single, as the patient was in good health more than two years afterwards.

There may be other evidences of tuberculosis in the body, such as advanced pulmonary disease, or, on the other hand, the liver may be exclusively or almost exclusively affected. When the abscesses are large enough to attract attention during life, their tuberculous nature cannot be ascertained until their contents have been bacteriologically examined. Tuberculous abscesses are usually small and multiple and belong to the group of local tuberculoses involving the bile-ducts.

EFFECTS OF TUBERCULOSIS ELSEWHERE IN THE BODY ON THE LIVER.

Tuberculosis elsewhere in the body may lead to other changes in the liver besides the secondary development of tubercles.

1. Focal necrosis and coagulation necrosis due to the virulent action of bacilli on the liver cells; this has been studied experimentally by Pilliet and is the same as that described by Hanot in other infective disorders.

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* Anderson, T. L.: The Australasian Medical Gazette, March 20, 1899, p. 93.
† Annals of Surgery, part cxxxiii, p. 98.
‡ Medical News, April 16, 1904, p. 727.
§ Mackenzie, H. W. G.: Trans. Path. Soc., vol. xli, p. 156.
‖ Waring, H. J.: Diseases of the Liver, Gall-bladder, etc., p. 108.
** Mayo Robson: Trans. Clinic. Soc., vol. xx, p. 83.

2. Fatty degeneration. The fatty liver met with in pulmonary tuberculosis is well known. It is described and discussed under Fatty Change in the Liver, page 423.

3. Lardaceous change is not uncommon in advanced cases where there has been long-continued suppuration. This change is due not to the tuberculous toxine, but in all probability to toxines derived from secondary infection of tuberculous abscesses or vomicæ with pyogenetic cocci.

TUBERCULOSIS AND CIRRHOSIS.

As has been already pointed out, portal cirrhosis is frequently complicated by tuberculosis. It has, however, been thought that tuberculosis may set up hepatic cirrhosis; in dealing with this question it will be clearer to consider it under two heads:

(A) Cirrhosis of the liver associated with tuberculosis of the liver.

(B) Cirrhosis of the liver associated with tubercle elsewhere, but not in the liver.

(*A*) *Cirrhosis Associated with Tuberculosis of the Liver.*—In a patient with latent cirrhosis of the liver generalised tuberculosis may of course arise, and miliary tubercles develop in the liver in common with the other viscera of the body. Tubercle bacilli may also be carried to a cirrhotic liver from the intestines. In children with nutmeg livers from backward pressure in heart disease secondary infection of the portal spaces with tuberculosis has been known to supervene. The amount of fibrosis is not great and the condition is essentially a complication of chronic venous engorgement of the liver; it is referred to under the name of "cardio-tuberculous cirrhosis" (p. 101). A large fatty and cirrhotic liver containing miliary tubercle is sometimes seen. The two processes of hepatic cirrhosis and tuberculosis are probably independent of each other, but are both disposed to by the same factors, viz., alcoholism.

Hanot and Gilbert * describe a large fatty liver with small-cell infiltration and fibrous hyperplasia of the portal spaces and miliary tubercles as a morbid entity, due to tuberculosis, under the names "hypertrophic fatty tuberculous hepatitis" or "hypertrophic fatty cirrhosis." Clinically there is enlargement of the liver, slight jaundice, and a little ascites, the disease running a rapid course in about six weeks. These authors further describe two less acute forms of tuberculous cirrhosis: (*a*) Without any enlargement of the liver, and (*b*) with more fibrosis than in the previous form, but with similar fatty change and tuberculous infiltration. The two latter forms only differ in the fact that one shows marked nodules, like those seen in cirrhosis with adenoma. There is no doubt that these forms occur, but I believe that, generally speaking, the cirrhotic changes are not due to the tuberculosis. Around tuberculous masses in the liver substance there is local fibrosis which sometimes spreads diffusely into the surrounding liver tissue.

On the other hand, it is quite reasonable to believe that tubercle bacilli might, under certain conditions, such as high resistance of the liver or a low degree of microbic virulence, give rise to fibrosis in the liver just as in the lungs. This does not very often happen in man, since if the resistance of the liver is good or the vitality of the bacilli feeble, the latter would probably be destroyed outright. Still there are experimental grounds for believing that tubercle bacilli may under some conditions have a sclerogenic effect on the liver. Hanot and Gilbert † found that in guinea-pigs the bacilli of avian tuberculosis produced a markedly cirrhotic liver with deep scars, while tubercle bacilli from man induced fatty change or coagulation necrosis. (Pilliet.‡) A small deeply scarred liver with lobulation and cicatrices like that of acquired syphilis has been found by Hanot to be associated with scattered miliary tubercles in the substance of the organ. It resembles, in fact, the lesion produced experimentally in guinea-pigs by avian tubercle bacilli.

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* Hanot and Gilbert: Archiv. général. de Méd., tome clxiv, p. 513.

† Hanot and Gilbert: Soc. de biolog., Jan. 30, 1892.

‡ Pilliet: Thèse de Paris, 1891.

The following case, recorded by Collet and Gallavardin,* may perhaps be regarded as an example of cirrhosis due to tuberculosis. In a woman aged sixty in whom the spleen (4½ pounds) showed massive tuberculosis the liver was greatly enlarged and showed small caseous tubercles in connexion with the portal spaces and a diffuse and rather delicate fibrosis. The hepatic changes were regarded as secondary to those of the spleen, and might be considered as an example of cirrhosis of splenic origin. (*Vide* p. 189.)

(*B*) *Cirrhosis Associated with Tuberculosis Elsewhere, but not in the Liver.*—This association of hepatic cirrhosis and tuberculosis elsewhere in the body is a common one; in most cases where the tuberculous process is active it has developed subsequently to the cirrhosis of the liver. In other instances there may be obsolete and latent tubercle of old date and independent cirrhosis of the liver, which are only discovered at the autopsy. In a certain number of cases old tuberculous lesions in the lungs are lighted up and make rapid progress in the course of alcoholic cirrhosis.

Nodular cirrhosis is sometimes found in fatal cases of pulmonary tuberculosis. Toxines generated in the lungs may lead to extensive fatty change in the proliferated liver cells forming the adenomatous projections in the cirrhotic liver. The appearance thus produced may imitate very closely that of multiple nodules of growth. It is conceivable that tuberculous lesions in other parts of the body may, by the production of chemical poisons, induce cirrhosis of the liver without any tuberculosis of that organ. Thus, in cases of pulmonary tuberculosis, in which streptococcal infection of cavities is very common, toxines may be absorbed from the suppurating surfaces and carried to the liver by the general circulation. In most cases of septic absorption from the lungs fatty degeneration in the liver without any fibroses results, but in very chronic cases it is conceivable that cirrhosis might be brought about. Again, expectoration when swallowed may not only be the source of toxic bodies, which may subsequently be carried to the liver by the portal vein, but may set up gastro-enteritis and follicular ulceration of the intestines, which is not necessarily tuberculous, and thus give rise to dyspeptic cirrhosis of the liver. Mouisset and Bonnamour,† however, believe that cirrhosis in tuberculous patients is nearly always due to concomitant alcoholism.

Hanot ‡ described lobulation of the liver in 7 cases of chronic tuberculosis and believed that fibrosis was due to the tuberculous toxine. I have notes of one such liver in a man with chronic phthisis in whom there was no history of syphilis and no gummata in the body; there was, however, a scar on the penis, and there can be little doubt that it was in reality syphilis. Possibly some of Hanot's cases may have been examples of tardive hereditary syphilitic disease of the liver with secondary tuberculosis. At any rate, it must be very rare, indeed, to find such a condition in tubercle pure and simple.

In conclusion, although from a pathological point of view tuberculosis, both in the liver and when confined to some other part of the body, may under certain circumstances set up some fibrosis in the liver, there is no reason to think that genuine cirrhosis of clinical importance is primarily produced in this way. Tuberculosis, whether in the liver or elsewhere, may produce degenerative changes in the liver cells, and when there is pre-existing cirrhosis, considerable damage may be done in this way.

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* Collet et Gallavardin: Archiv de Méd., expériment. et d'Anat. path., Mar., 1901.

† Rev. de Méd., 1904, p. 337.

‡ Hanot: Gaz. des Hôp., 1893, p. 902.

SYPHILITIC DISEASE OF THE LIVER.

History.—That syphilis affects the liver is a very ancient idea; according to Frerichs,* as old as the history of syphilis itself. But the earlier views naturally differed from those of the present day. Fallopius † in the sixteenth century considered that the liver was primarily affected in syphilis and so corrupted the humours of the body that ulcers occurred on the genitals. Subsequently Morgagni opposed the view that the liver was affected in syphilis. Later Van Swieten, Portal, and Ricord described syphilitic lesions of the liver, but very little attention was directed to the visceral lesions of syphilis until Dittrich ‡ in 1849, and Sir S. Wilks § in this country, described gummata in the internal organs. The distinction between gummata and nodules of malignant growth dates from this time; previous to Wilks' observations gummata were regarded as cancerous nodules or even as evidence of healing of malignant growths.

The subject of syphilitic disease of the liver will be considered under the two main heads of (i) the acquired and (ii) the congenital or hereditary forms.

HEPATIC LESIONS IN ACQUIRED SYPHILIS.

The hepatic changes due to acquired syphilis will be considered under the heads of (i) the secondary and (ii) the tertiary manifestations, while the briefest reference only will be made to the possibility that remote—parasyphilitic—changes in the liver may be referred to syphilitic infection.

THE SECONDARY MANIFESTATIONS OF SYPHILIS IN THE LIVER.

The diffuse pericellular cirrhosis of congenital syphilis is generally regarded as being pathognomonic and as not occurring in the acquired form. Whether pericellular cirrhosis is so entirely limited to the congenital form may be very seriously questioned. That it is seldom found except in that disease is true enough, but it must be remembered that congenital syphilis is much more often fatal than the acquired disease in any stage, so that opportunities for examining the liver in the secondary stage of acquired syphilis only occur in rare and accidental instances, and that hepatic manifestations of acquired syphilis are less frequent than those of the congenital affection.

Sir Hermann Weber ‖ many years ago described a case of acquired syphilis in a man aged twenty, in whose liver the lesions appear to have been pericellular. I have examined a few cases in which the liver of syphilitic subjects has shown diffuse pericellular cirrhosis without there being any gummata present. In other cases pericellular cirrhosis may be seen at a considerable distance from gummata.

Since then few cases are examined during the secondary stage, and since it is a lesion from which recovery is quite possible, it is not unlikely

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* Frerichs: Diseases of Liver (Transl. New Sydenham Soc.), vol. ii, p. 150.

† Fallopius: Tract. de Morbo Gallico.

‡ Dittrich: Prager Vierteljahresschrift, 1849, S. 1; 1850, S. 33.

§ Wilks, S.: Trans. Path. Soc., vol. viii, p. 240.

‖ Weber: Trans. Path. Soc., vol. xvii, p. 152.

à priori that the condition occurs temporarily and usually passes away. As an argument in support of this it may be pointed out that in those rare cases of acute yellow atrophy supervening after syphilis the microscopic appearances are at least compatible with the view that there has been pericellular cirrhosis and that excessive necrosis of the hepatic cells has supervened.

In a man aged forty-seven, who died of cerebral hæmorrhage and had gummata in his testes, the liver showed very diffuse intercellular fibrosis which varied in different areas, but was compatible with the views that there had been partial acute atrophy with recovery, or that it was intercellular cirrhosis. In describing this specimen Dr. Parkes Weber,* who kindly showed the slides to me, drew attention to the fact that the situation of the fibrosis, viz., around the capillaries of the hepatic artery, resembled that of lardaceous change and pointed to the poison being carried by the hepatic artery.

The views as to an anatomical substratum of the jaundice occurring during the exanthematous stage will be referred to directly. Finger,† and Adami‡ suggest that it is a generalised toxic disturbance of the organ, which may or may not lead to the generalised intercellular cirrhosis characteristic of congenital syphilis. If this toxic disturbance is excessive, necrosis of the hepatic cells may follow and give rise to icterus gravis. (*Vide* Acute Yellow Atrophy in the Course of Syphilis.) In exceptional instances gummatous lesions have been found in the liver during the period of secondary manifestation. (*Vide* p. 358.)

To sum up, in acquired syphilis the liver may be affected in the secondary stage so as to give rise to jaundice, either innocent or malignant; while anatomical changes allied to or resulting in pericellular cirrhosis and underlying the clinical manifestations must not be forgotten.

Jaundice in the Secondary Stage of Syphilis.—Jaundice may occur early in the secondary stage at the same time as the cutaneous roseola. Gubler § in 1853 first drew attention to this association in a memoir containing five cases. It is, however, uncommon, and more so in Germany than in France; in 15,799 cases of syphilis S. Werner ‖ met with jaundice in 57, or only 0.37 per cent. In 1868 Lancereaux ** collected 21 cases, and in 1900 Lasch†† referred to 49 cases, almost all from French literature. These figures would suggest that jaundice during the roseolous stage is far rarer than it is in reality.

It must be admitted that there are more theories to explain the occurrence of jaundice in the early stages of syphilis than facts to appeal to. Inasmuch as it coincides with the exanthem, it was first thought that it is due to a somewhat similar condition, in the mucous membrane of the bile-duct (Gubler); or, in other words, a specific catarrhal cholangitis. A condyloma of the bile-duct has also been suggested.

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* Weber, F. P.: Brit. Med. Journ., 1899, vol. i, p. 728.
† Finger: Die Syphilis u. d. vener. Krankh., 1892.
‡ Adami: New York Med. Journ., April 22, 1899.
§ Gubler: Mem. Soc. biolog., vol. v, p. 235, 1853.
‖ Werner, S.: München. med. Wochen., 1897.
** Lancereaux: Syphilis, vol. i, p. 182. In New Sydenham Soc. Library.
†† Lasch, O.: Berlin. klin. Wochen., 1894, S. 904. Selected essays, New Sydenham Soc. Library, 1900, p. 145.

According to another view, pressure is exerted on the ducts by syphilitic enlargement of the lymphatic glands in the portal fissure; in favour of this it may be mentioned that out of Werner's 57 clinical cases of syphilitic jaundice there was marked enlargement of the superficial lymphatic glands in 41.

In Talamon's * case of acute yellow atrophy in a girl aged seventeen with a secondary cutaneous eruption and other signs of syphilis the glands in the portal fissure were enlarged but did not compress the common bile-duct.

It is probably not simply catarrhal jaundice occurring in a person who has recently contracted syphilis, since the successful treatment is that of syphilis and not of catarrhal jaundice. The most probable explanation of the jaundice is a catarrhal condition of the small intrahepatic bile-ducts which is merely part of a general syphilitic hepatitis. The change in the liver is probably a pericellular infiltration with small round cells, like that seen in hereditary syphilis. When this change is excessive, it may run on into acute yellow atrophy. There is no proof that the jaundice is due to the administration of mercury, for in only 4 of 49 cases of benign jaundice occurring in the early stage of syphilis, collected by Lasch, had mercury been given before the icterus appeared.

Sex.—It is seen in about an equal number of men and women; in Lasch's 49 cases 25 were men and 24 women, but as more cases of syphilis are seen in men, syphilitic jaundice is proportionately more frequent in women.

Its onset is usually sudden without any apparent cause and is not accompanied by any special disturbance, such as is seen in cholelithiasis or catarrhal jaundice. It comes on simultaneously with the cutaneous roseola and may coincide with a particularly copious eruption. It may appear as soon as five weeks after infection, or later up to the sixth month.

Clinical Features.—The jaundice is well marked, and unless treated with mercury, tends to become chronic; thus it may last three months if treated with the ordinary remedies for catarrhal jaundice. The aspect of the patient with a jaundiced syphilitic eruption is very characteristic and somewhat repulsive. There is an absence of gastro-intestinal symptoms and the appetite is well preserved, though distaste for fatty food may be experienced. The liver is usually slightly enlarged and the spleen may be palpable.

Diagnosis.—The important point is to recognize that in a patient with recent syphilis jaundice may be a specific manifestation and not an independent attack of catarrhal jaundice. From the presence of the roseola and enlarged glands the recognition of syphilis is easy.

The treatment is that of secondary syphilis; it is noteworthy that the ordinary treatment of catarrhal jaundice is without any good result. If the mercurial treatment is prematurely discontinued, jaundice may recur.

The *prognosis* is good, as a rule, but in some rare cases the jaundice passes into acute yellow atrophy. There are probably intermediate grades between the benign jaundice and the acute yellow atrophy occurring in the early stage of syphilis.

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* Talamon: La Médecine Moderne, Feb. 13, 1897.

THE TERTIARY LESIONS OF SYPHILIS IN THE LIVER.

The specific tertiary lesions in the liver are polymorphic and include gummata, gummatous infiltration, cicatrices, and a combination of gummata and cicatrices (sclero-gummatous form). Lardaceous disease, which may be considered as a parasyphilitic lesion, is often combined with gummata and with cicatrices.

The manifestations of tertiary syphilis in the liver may be divided into (*a*) those that are progressive and (*b*) those that are merely the relics of past syphilitic activity. In other words (*a*) the late secondary and tertiary lesions seen in the gummata and gummatous infiltration of the organ and (*b*) the cicatrices, calcified remains, and deformities left behind by the first-named lesions are both included under the tertiary manifestations. Lardaceous disease, which is such a well-known sequela of syphilis, is dealt with elsewhere. (*Vide* p. 430.)

GUMMA.

The word gumma was employed in its present sense by Fallopius in the sixteenth century in his Tractatus de Morbo Gallico.* But it was not generally used until comparatively recent times. In his work on the liver in 1857 Budd † gave a careful description of gummata under the name of "encysted knotty tumours of the liver," and separated them from cancerous growths, with which they had been generally confounded, but did not recognise their syphilitic origin or speak of them as gummata.

Method of Formation of Gummata.—In the early or secondary stage the future gumma is a mass of syphilitic granulation tissue of a pink colour, sharply localised, and contrasting with the healthy liver substance. At this stage it is better to speak of it as a syphiloma, since the term gumma describes a central mass of caseous material surrounded by a fibrous capsule. After a time necrosis occurs in the centre of the syphiloma; this is partly due to syphilitic endarteritis in the neighbourhood whereby the blood-supply is cut off, and probably in part to an increase in amount or concentration of the syphilitic poison which kills the granulation tissue of the syphiloma. At this stage there is a yellowish-white centre surrounded by pink granulation tissue. Later the syphiloma of the secondary stage is transformed into a caseous mass surrounded by a fibrous capsule, a condition resembling a caseous tubercle of some duration. By the union of several small gummata a large gummatous area may result.

Structure, etc.—A well-marked gumma consists of a firm, yellowish-white mass, not unlike cheese, surrounded by a fibrous capsule which spreads out for a short distance into the surrounding liver tissue. In rare instances the caseous part of gummata is yellow from bile-staining.

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* Fagge and Pye Smith: (Ed. i, 1886), vol. i, p. 123.

† Budd: Diseases of the Liver, p. 416, ed. iii, 1857.

(Marie.)* There are thus three zones in a gumma: (1) The central area of necrosed or necrosing granulation tissue; (2) the surrounding fibrous capsule; (3) the invasion of the surrounding parts of the liver by interstitial fibrosis.

Old gummata consist of the central caseous portion and the well-formed fibrous capsule, there being no advancing margin. In recent gummata where the capsule is indefinite there is, on the other hand, well-marked infiltration of the liver tissue, the lesion being progressive.

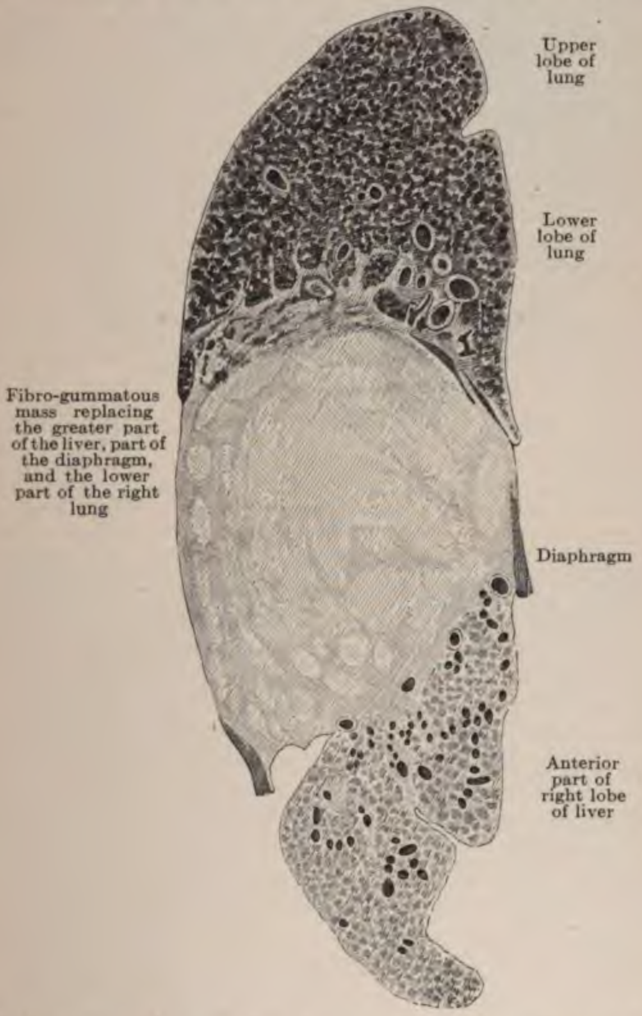
Upper lobe of lung
Lower lobe of lung
Fibro-gummatous mass replacing the greater part of the liver, part of the diaphragm, and the lower part of the right lung
Diaphragm
Anterior part of right lobe of liver

FIG. 41.—A LARGE GUMMA OF THE LIVER EXTENDING THROUGH THE DIAPHRAGM INTO THE LOWER LOBE OF THE RIGHT LUNG.
From a specimen (Series ix, 183 g) in St. George's Hospital Museum.†

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* R. Marie: Bull. Soc. Anat. Paris, 1901, p. 625.

† I am indebted to Professor S. Delépine for this block, which appeared in the Transactions of the Pathological Society of London, vol. xlii, p. 151.

The amount of fibrous tissue enclosing a gumma varies; with large and advancing gummata it may be slight and indistinct, with old gummata it is firm and dense. As it contracts it presses on the caseous centre, and at the same time, if near the capsule of the liver, produces thickening, puckering, and cicatrices on the surface of the organ. Perihepatitis and thickening of the capsule are thus produced; in rare instances, of which an example is given on page 168, there may be chronic universal perihepatitis. Adhesions frequently form between the liver and adjacent organs, the diaphragm and the anterior abdominal wall; in rare instances gummatous change may behave like malignant disease and invade the anterior abdominal wall or the diaphragm.

In a specimen (series ix, 183 g) in St. George's Hospital Museum an immense gumma of the right lobe of the liver passed through the diaphragm and extensively infiltrated the lower lobe of the right lung (Delépine and Sisley*). (*Vide* Fig. 41.) In a case of late hereditary syphilis with the usual tertiary changes, recorded by Post,† gummatous inflammation extended into the anterior abdominal walls and produced a definite tumor.

The naked-eye appearances of caseous gummata may sometimes closely resemble those of certain cases of primary massive carcinoma and multiple carcinomatous growths in the liver.

Gouget ‡ has described a case in which columnar-celled carcinomatous growths were at first thought to be gummata; I have seen similar appearances on several occasions. As a rare coincidence secondary growths may occur in a liver containing gummata. Microscopical examination is necessary before one can be certain that both gummata and secondary new-growths are present. In 1891 I examined such a case; a man had primary carcinoma of the colon with small secondary growths in a scarred and gummatous liver. The left testis also contained gummata.

The microscopic appearances of a gumma present differences according to the age of the formation. In the stage when caseation has begun the central necrotic part, which to the naked eye appears white, is fibrillar or granular, shows a few nuclei but is otherwise structureless, and does not take the stain properly; around it there is granulation tissue, which occasionally contains giant cells. These giant cells, which are rare in gummata, are formed by the union of pre-existing young connective-tissue cells, probably in order to absorb the caseous débris. It is noteworthy that the giant cells seen in gummata are not so large or so well developed as those seen in tuberculosis. Necrosis and caseation may be seen to be extending into this surrounding granulation tissue in young or recent gummata, while in older ones organization is going on and a capsule of connective tissue is formed around the caseous mass. The fibrous capsule contains elastic fibres and if stained with osmic acid shows globules of fat.

The granulation tissue spreads into the surrounding liver tissue for a short distance, so that there is intercellular cirrhosis in the immediate neighbourhood of the gumma. Later groups of liver cells become surrounded by bands of young connective tissue, and in recent cases the solid columns of small cubical cells which stain deeply are prominent objects at the margin of a gumma. These pseudobile canaliculi are very probably due to compensatory hyperplasia of the liver cells. The liver cells near the margin of a gumma are flattened from pressure and may be spindle shaped.

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* Delépine and Sisley: Trans. Path. Soc., vol. xlii, p. 141.

† Post: Boston City Hospital Reports, 1898, p. 233.

‡ Gouget: Bull. Soc. Anat. Paris, 1898, p. 605.

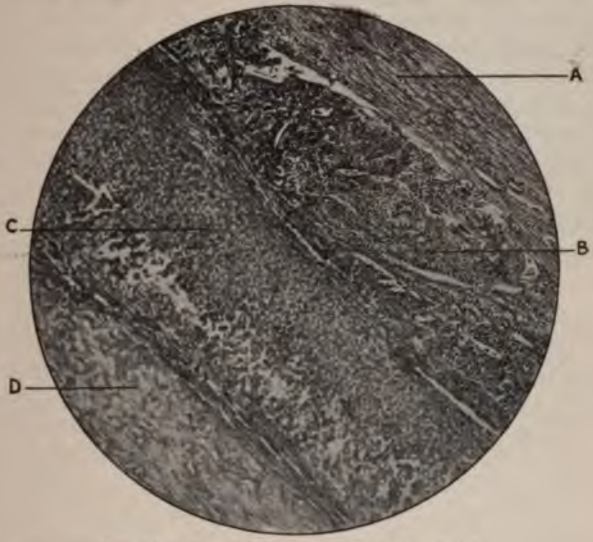

FIG. 42.—RECENT GUMMA OF LIVER. × 30.
A, fibrous capsule; B, syphilitic granulation tissue; C, caseating granulation tissue; D, caseous centre.

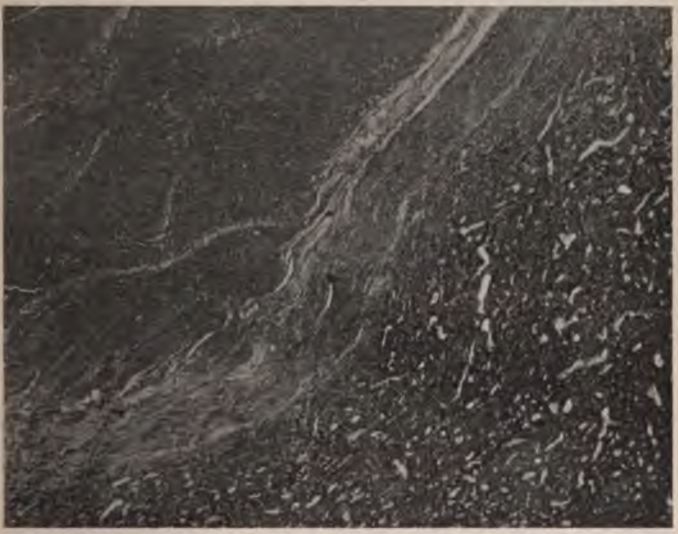

FIG. 43.—OLD GUMMA OF LIVER.
The lighter part is the caseous material; it is surrounded by a dense fibrous capsule which extends into the surrounding liver substance. (Photomicrograph by S. G. Penny, Esq.)

The small arteries at the margin of a gumma show well-marked endarteritis obliterans. There is sometimes lardaceous change immediately around the gumma. In old gummata, where the lesion is no longer advancing, the fibrous capsule is dense and well formed and there is no small-cell infiltration around the gumma, while giant cells are not seen. Particles of calcareous salts may be seen in the caseous material or in the surrounding fibrous tissue. The caseous material and the proliferating zone around it contain a good deal of fat and thus differ from tuberculous caseation, in which fatty change is slightly marked, the degenerative change being of a hyaline nature. (Gaylord and Aschoff *.)

Retrogressive Changes in Gummata.—The caseous material may diminish in amount from the circumferential pressure exerted upon it by the contraction of its fibrous capsule; at the same time it becomes drier from absorption of fluid. Calcification may then occur. A certain amount of calcareous change is not very rare, but it is usually only in small particles which do not offer any real resistance to the knife. In these cases the presence of calcareous matter is best seen on making microscopic sections of the gumma. In other instances calcification is best seen in the capsule of the gumma. (*Vide* Cambridge Museum, Nos. 504, 505.) In exceptional cases calcification is very prominent.

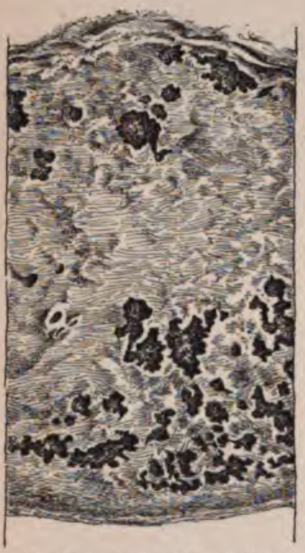

Fig. 44.—Section of Liver Showing Diffuse Calcification Probably Subsequent to Gummatous Infiltration.

St. George's Hospital Museum, Series ix. 172 B. (Drawn by Dr. E. A. Wilson.)

Dr. Fooks kindly sent me the liver of a woman aged fifty-nine who died in the Brentford Union Asylum, Isleworth, in April, 1898. It weighed 31½ ounces and was two-thirds the natural size. The surface was scarred and puckered all over, especially on the right side. These cicatrices were all calcified, and on cutting into the organ several calcareous masses the size of a walnut were found.

Targett † showed before the Pathological Society a specimen of diffuse calcification of the liver which probably supervened on gummatous change. A slice of this liver is in St. George's Hospital Museum. (*Vide* Fig. 44.)

Calcification of the liver may in very rare instances occur independently of syphilis (*vide* p. 437) and is met with in animals. There is a dried section of a horse's liver showing infiltration with carbonate and phosphate of lime in St. Bartholomew's Hospital Museum (No. 2239).

Occasionally gummata may soften down; this may very probably be the result of treatment with iodides and be a stage in the process of absorption. It may also be due to septic infection, and when it occurs in a large gumma the condition is practically a chronic abscess.

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* Gaylord and Aschoff: Pathological Histology, p. 95.

† Targett: Trans. Path. Soc., vol. xl, p. 123.

Moxon* described a large gumma, which softened down and communicated with a bile-duct. In former days gummata have actually been described as "retiring abscess of the liver" (*vide* Cambridge Museum, No. 503), and were supposed to be due to concentration and solidification of material originally fluid.

Unless the gumma is very large, it slowly undergoes absorption. This is carried on by phagocytosis and depends on the neighbouring blood-vessels and lymphatics being permeable and not obstructed by syphilitic changes. The more the gumma contracts, the more it resembles the scars and cicatrices which are in many cases the only remains of obsolete gummata. This probably accounts for the rarity of gummata in old persons. The scars may, however, result from the organization of inflammatory products without any central caseation having taken place.

Number and Striation.—Gummata may be circumscribed and multiple, or there may be diffuse gummatous infiltration of a large part of one or even of both lobes. The right lobe is much more often affected and the anterior surface far more frequently than the under aspect. They are much more often multiple; in 86 cases of hepatic gummata collected by J. L. Allen † only 11 were single. It is said that the neighbourhood of the falciform ligament is a favourite situation for gummata, but in my experience I have not noticed any such special localisation of gummata except the anterior surface. They may occur in any part and may, when present in an exceptional position, *i. e.*, near the portal fissure, press on the main trunks or branches of the bile-ducts or portal vein.

SYPHILITIC CICATRICES.

Deep furrows on the surface of the liver, due to cicatricial contraction, are the result of organisation of syphilitic granulation tissue. Cicatrices may be formed directly from syphilomata or be the last stage of a gumma which has undergone absorption. The cicatrices may be linear or may be star-like. The linear cicatrices may divide a lobe into a number of lobules; the star-like cicatrices are depressed with well-formed fibrous tissue radiating into the capsule on all sides of it. The liver may be so widely fissured and lobulated by cicatrices that it has a slight resemblance to the coarse, hobnailed liver of portal cirrhosis, but the irregularity of this diffuse syphilitic fibrosis or "syphilitic cirrhosis," as it is often called, distinguishes it from genuine portal cirrhosis. Like gummata, these scars are said to be frequent in the neighbourhood of the falciform ligament. When they occur around the portal fissure, they may involve the portal vein, giving rise to ascites, or the bile-ducts, thus producing jaundice; or if they occur near the coronary ligament, they may lead to narrowing or obliteration of the hepatic veins (*vide* p. 49).

Bosanquet,‡ who records a case of obliteration of the inferior vena cava by syphilitic cicatrices spreading from a gummatous liver, could not find any other published instances of syphilitic obstruction of the inferior vena cava.

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* Moxon: Trans. Path. Soc., vol. xxiii, p. 153.

† J. L. Allen: Unpublished Thesis for M. B. degree, Cambridge, 1899.

‡ Bosanquet, W. C.: Edinburgh Medical Journ., New Series, vol. xii, p. 250, Sept., 1902.

The scars may contain a central caseous mass, showing that they are receding gummata; sometimes calcification has commenced in the caseous material. The older the scar, the denser it is, and the more depressed the surface of the liver over it.

GUMMATA AND CICATRICES COMBINED (SCLERO-GUMMATOUS FORM).

The contraction of syphilitic cicatrices and gummata may lead to great deformity, so that the organ is nodular and irregularly lobulated. Such lobulation must not be regarded as persistence of a congenital condition, for the liver is not, like the kidney, normally lobulated in the fœtus.

In a girl aged twenty-five years who died under my care in St. George's Hospital with syphilitic stenosis of both bronchi * the liver (52 ounces) was occupied by multiple caseous gummata and was so extensively scarred that as many as 16 lobes could be counted on its anterior surface.

The shape of the liver may be altered out of all recognition. The relative size of the two chief lobes of the liver may be greatly altered; thus, the left lobe may be almost entirely destroyed by fibrous contraction or enlarged from gummatous infiltration, while in some cases it may be enlarged from hyperplasia of the liver substance to compensate for extreme destruction of the right lobe. As a rule, the syphilitic changes and enlargement are much more marked in the right than in the left lobe.

Association of Gummata and Lardaceous Change in the Liver.—As already pointed out, local lardaceous change may be found around a gumma. In other instances gummata may be found in a universally lardaceous liver. In 86 cases of gummata collected by J. L. Allen the liver was lardaceous in 12, or 14 per cent.

Incidence of Gummata in Universally Cirrhotic Livers.—It might naturally be supposed, since alcoholic excess and exposure to syphilitic infection, or, as Osler puts it, the worship of Bacchus and Venus, are frequently associated, that gummata would be common in universally cirrhotic livers. This, however, is not the case, and it is remarkable how seldom gummata and ordinary portal cirrhosis coëxist in the same liver.

In 86 cases of hepatic gummata collected by J. L. Allen only 4 were combined with genuine cirrhosis. In Flexner's † 88 cases of hepatic syphilis these conditions were combined in 9 instances.

A certain amount of fibrosis is usually present in the liver tissue immediately surrounding a gumma, and cicatrices leading to scarring and lobulation of the organ may be associated with gummata, but genuine multilobular cirrhosis is rare.

INCIDENCE OF TERTIARY HEPATIC LESIONS.

Though well recognized and exhaustively described, the tertiary hepatic manifestations are by no means very common. It is true that cicatrices of old gummata are usually entirely latent, so that they are less frequently detected clinically than in the postmortem room. Cicatrices are apparently more often seen than gummata, though in many instances gummata and cicatrices are of course present in the same liver. But even in the postmortem room they cannot be said to be common.

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* *Vide* Trans. Clinic. Soc., vol. xxxii, p. 158.

† Flexner: New York Med. Journ., Jan. 18, 1902, p. 101.

In a critical examination of the postmortem records of St. George's Hospital, dealing with a period of forty-two years (from 1857 to 1898), J. L. Allen only found 37 cases of undoubted hepatic gummata; during this same period there were 11,629 autopsies; there were, in addition, 27 other cases in which cicatrices alone were present. In a period of thirty-five years during which there were 5088 autopsies at the Philadelphia Hospital, Flexner * found that gummata were present in 23 cases, cicatrices in 38, and in all 88 cases of hepatic syphilis, half this number being cases of diffuse syphilitic fibrosis.

There is indeed a great contrast between the frequency of hepatic lesions in congenital and in acquired syphilis.

Predisposing Causes.—It has been thought that previous disease of the liver or conditions such as alcoholism, malarial infection, or a previous attack of jaundice, would, by diminishing the resistance of the liver, render it more likely to be affected. Traumatism, such as blows or previous injury to the liver, may very probably, as elsewhere in the body, determine the occurrence of gummata in the organ. It is interesting to note that gummata have been found in the pendulous portion of the right lobe seen in the tight-laced or corset livers of women. In this connexion it would be interesting to know what proportion of cases of hepatic gummata occur in women.

In 83 cases of gummata of the liver collected from various sources by J. L. Allen, 60 were males and 23 females; he could not find any evidence to support the hypothesis that tight lacing disposed the liver to gummatous change.

It is difficult to prove anything with regard to the influence of trauma in determining the incidence of gummata in the liver, but the greater frequency of hepatic gummata in the male sex, nearly 3 to 1, and the fact that gummata are more commonly met with on the anterior surface of the liver, are certainly in favour of this hypothesis.

In a case recorded by Pitt † the irritation of an old hydatid cyst in the liver seemed to have determined an extensive syphilitic formation around it.

ETIOLOGY.

Age Incidence.—The great majority of hepatic gummata are found between the ages of twenty-five and fifty years. In 78 cases of hepatic gummata collected by J. L. Allen, 69, or 88.5 per cent., occurred within this limit. The average age of these 78 cases was thirty-nine years, and was almost the same in the two sexes. The cases were arranged as follows:

AGE.	NUMBER OF CASES.	AGE.	NUMBER OF CASES
15–20	1	46–50	11
21–25	2	51–55	3
26–30	15	61–65	1
31–35	10	66–70	1
36–40	21	71–75	1
41–45	12		

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* Flexner: New York Medical Jour., 1902, p. 101.

† Pitt: Trans. Path. Soc., vol. xxxvii, p. 276.

Gummatous disease in the liver has been observed at the advanced age of eighty-nine (Wagner*).

Interval between Infection and the Appearance of Gummata.—Usually a number of years, from ten to twenty, elapse between the primary chancre and evidence of gummata in the liver; but exceptionally gummata have been found within a year of infection.

Key † found a gumma the size of a walnut in the liver of a woman aged twenty-six who died of generalised tuberculosis six months after infection; and Fleischhauer,‡ a gumma in the liver of a man who died seven months after infection. These cases are analogous to the occurrence in rare instances of gummata in the livers of fœtuses and still-born children. (*Vide* p. 370.)

CLINICAL MANIFESTATIONS.

Clinically the occurrence of manifestations due to hepatic lesions, apart from lardaceous disease, is comparatively rare in the subjects of tertiary syphilis.

Mauriac,§ combining the statistics of Fournier, Ehlers, and Hjalmann, found that in 7497 cases of tertiary syphilis symptoms pointing to the liver occurred in only 41.

It is remarkable how rare syphilitic lesions in the liver are in cases of locomotor ataxia, and it has been suggested that there is some kind of antagonism between hepatic syphilis and parasyphilitic lesions of the nervous system. Gummata and especially cicatrices are not uncommonly latent, and are only found after death as a surprise.

The factors which determine the development of symptoms are: (1) the size and extent and (2) the position of syphilitic lesions in the liver.

1. If a gumma is large, it will give rise to the signs of a tumor, and by irritating the capsule of the liver to perihepatitis and pain, while the morbid metabolism going on inside it may lead to the production and absorption of poisons which will lead to constitutional symptoms, such as anæmia, asthenia, and perhaps fever.

2. A cicatrix or small gumma on the convexity of the liver need give rise to no symptoms, but if situated in the portal fissure, jaundice and ascites may follow.

There is a great difference between the relative importance of the symptoms produced by a caseous gumma and by an old cicatrix; for symptoms due to the pressure of a gumma may be relieved, or disappear under the influence of iodides, whereas it is highly improbable that an old cicatrix will be altered by such treatment.

As has just been pointed out, there is usually a very considerable interval (ten to twenty years) between the onset of symptoms and the primary infection; it may be postponed for thirty or forty years; so that it has been said that no one can be regarded as cured of syphilis until he has been examined postmortem. Some cases show signs of hepatic involvement within three years of infection, and exceptionally hepatic symptoms develop with great rapidity. In the early stages of tertiary syphilitic disease of the liver, before very definite localising symptoms and signs appear, there is very commonly weakness, general loss of health, failure of appetite, and gastro-intestinal symptoms. According to Marcuse,* two-thirds of the cases show gastro-intestinal symptoms in the early stages. As gummata nearly always reach the surface of the liver, a certain amount of local perihepatitis is common, which, according to its intensity, accounts for feelings of discomfort, pain, and tenderness in the right hypochondrium; the pain may radiate up to the right shoulder, and is sometimes accompanied by local tenderness. Pain is one of the most frequent symptoms in tertiary syphilis of the liver.

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* Wagner: Archiv der Heilkunde, Bd. v, S. 126, 1864.

† Key: Schmidt's Jahrb., 1874, Bd. 161.

‡ Fleischhauer: XII. Congress f. inn. Med., Wiesbaden, 1893.

§ Mauriac: Gaz. hebdom. de Méd. et de Chirurg., 1888.

The clinical manifestations of tertiary syphilitic disease of the liver vary, and may for convenience be grouped under different headings:

(I) Where the symptoms suggest portal cirrhosis, or simple chronic peritonitis and perihepatitis.

(II) Presenting the features of widespread lardaceous disease.

(III) Suggesting tumor of the liver, such as malignant growth, hydatid, or enlarged gall-bladder.

(IV) Imitating suppuration in the liver.

(V) Resembling cholelithiasis.

(VI) Resembling chronic splenic anæmia.

(VII) Where the clinical features resemble hypertrophic biliary cirrhosis.

I. **Cases Imitating Cirrhosis.**—These cases are frequent and important, as they probably account for some of the reputed cures of ordinary cirrhosis. There is ascites which is serous, but in rare instances has been noticed to be chyliform (Veil, Galvagni,† Poljakoff ‡) or even hæmorrhagic. Other signs of portal obstruction, such as hæmatemesis, dilated veins in the abdominal walls, and dyspepsia, are much less frequent than in cirrhosis. There may be enlargement of the spleen. Jaundice is very infrequent. Ascites may be produced in several ways: (i) by the pressure of cicatrices or gummata on the intrahepatic branches of the portal vein, or in some instances on the trunk of the vein in the portal fissure of the liver; (ii) by constriction of the hepatic veins; (iii) by perihepatitis over gummata; this is usually local, but may be more widespread and give rise to some chronic peritonitis.

Under iodide of potassium the gumma undergoes absorption and the symptoms will pass off unless there is enough cicatricial tissue left to exert permanent pressure on the portal vein or its branches. In a number of cases the absorption of the gumma leads to relief; these cases are responsible for some of the reputed cures of portal cirrhosis, for iodides are commonly given in that disease. In other instances where there is no means of telling that there is a firm cicatrix, and not a gumma, embarrassing the portal circulation, antisyphilitic treatment fails, and the case more closely resembles common cirrhosis.

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* Marcuse: Wien. med. Wochen., Nov. 17, 1900, S. 2219.

† Veil, Galvagni: Quoted by Boix: Archiv. Général. de Méd., May 23, 1903, p. 1302.

‡ Poljakoff: Berlin. klin. Wochen., Jan. 1, 1900.

The Differential Diagnosis of Portal Obstruction due to Syphilitic Disease of the Liver from Ordinary Cirrhosis.—The history and the presence of other signs of syphilis should always suggest syphilitic disease of the liver and lead to adequate antisyphilitic treatment. In syphilis the liver may be irregularly enlarged, especially the right lobe, while in cirrhosis enlargement, if present, is more uniform. Definite enlargement of the spleen in the absence of lardaceous disease, which itself points to syphilis and should then be accompanied by albuminuria, is rather in favour of cirrhosis. An alcoholic history and dyspepsia of long standing are also in favour of cirrhosis. Ascites which recurs after paracentesis is probably not due to cirrhosis, but to chronic peritonitis and perihepatitis or to syphilitic disease of the liver. When ascites is due to cirrhosis, the patient is usually thin or emaciated, while in syphilitic disease of the liver nutrition may be fairly well preserved.

Cases Resembling Simple Chronic Peritonitis and Perihepatitis.—Cases of syphilitic disease of the liver in which ascites recurs will closely resemble simple chronic peritonitis, of which chronic universal perihepatitis is only a part. Chronic and recurrent ascites only occurs in a certain proportion of the cases of hepatic syphilis, while it is a constant feature in simple chronic peritonitis. There must, therefore, be undoubted evidence of syphilis in the body, or enlargement and irregularity of the liver, which point to gummatous disease rather than to universal chronic perihepatitis, before the diagnosis of syphilitic disease is made offhand in preference to chronic peritonitis. The effect of a thoroughly efficient course of iodides should, however, always be tried to settle the question of diagnosis. But the fact that the treatment fails does not absolutely put syphilitic disease out of court. Universal chronic perihepatitis may in some rare instances be associated with and possibly due to syphilis. (*Vide* Perihepatitis, p. 167.) Cheadle * considers that syphilis is the most important cause of perihepatitis. My own experience is that syphilitic gummata commonly give rise to local perihepatitis and thickening of the capsule, but that syphilitic infection is quite an exceptional cause of universal perihepatitis. In 22 cases collected by Hale White† syphilis was the apparent cause in 3.

II. **Cases with the Features of Lardaceous Disease.**—When a gummatous liver is associated with lardaceous disease, the renal affection gives rise to albuminuria and dropsy, and the aspect of the case may be that of renal disease. Under these circumstances the presence of a gumma in the liver may naturally not be suspected. The presence of albuminuria in syphilis is not, however, to be regarded as undeniable proof of lardaceous disease, though very suggestive of this change, since it may be due to a syphilitic nephritis. In some cases where the liver and spleen are both very considerably enlarged, the clinical aspect has been described as that of Hanot's hypertrophic biliary cirrhosis but without jaundice. (Boix.*)

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* Cheadle: Some Cirrhoses of the Liver, 1900, pp. 41, 43.

† Hale White: Allbutt's System of Medicine, vol. iv, p. 121.

The following is a well-marked case of syphilitic gummata of the liver combined with lardaceous disease:

Large Gumma in the Liver; Extensive Lardaceous Disease; Albuminuria; Ascites, Paracentesis; Peritonitis.—A man aged forty-two years was under my care in August–September, 1900, in St. George's Hospital, with ascites, albuminuria, and casts; there was no trace of jaundice and his facial aspect was that of cirrhosis. There was no cardiac disease or hypertrophy; the tension of the pulse was low. It was thought possible that he had lardaceous disease of the kidneys and syphilitic disease of the liver, but the diagnosis was open to doubt, as there was no history or signs of lues veneris. The testes were not enlarged and there were no scars in any part of the body. The spleen could not be felt. The liver was felt to be somewhat enlarged. He was put on iodide of potassium, but without any improvement, and his abdomen was tapped; a week later he vomited, complained of abdominal pain, and as there was considerable ascites, he was again tapped; the fluid withdrawn was turbid and contained numerous pus corpuscles; the patient got rapidly weaker and died on September 6. At the autopsy there were recent peritonitis and extensive lardaceous disease of the viscera. The liver weighed 8 pounds 10 ounces, was somewhat scarred, and showed a large gumma in the posterior part of the right lobe which was the size of a cocoanut; it compressed the right branch of the portal vein and had running through its centre a large bile-duct. There were other small gummata in the liver, which was lardaceous. The spleen, 20 ounces, was in a condition of diffuse waxy change. The left kidney was atrophied: the right weighed 15 ounces and was lardaceous.

III. **Gummata, etc., Imitating Hepatic Tumors.**—When, as they usually are, gummata are situated on the anterior surface of the liver, the irregularities they give rise to may be readily felt through the abdominal wall. The elevations of the liver substance due to the contraction of cicatrices are also easily palpable. A large gumma or gummatous infiltration of a lobe or part of a lobe may give rise to the suspicion of primary massive carcinoma, but if watched for a short time it will be seen that it does not enlarge at the same rate that a growth would. Iodides in full doses and mercury should be given in the absence of strong evidence that the enlargement is of a malignant nature. Jaundice and ascites, especially together, are more likely to be met with in malignant disease; other points in favour of growth are rapid increase in the size of the liver, marked constitutional symptoms, and, of course, any signs of a growth elsewhere. In a syphilitic subject enlargement and irregularity of the liver may be due either to gummatous disease or to new-growth, for syphilis, of course, in no way protects against malignant disease. The vigourous administration of iodides and mercury should decide the question, diminution in size of the liver settling the diagnosis in favour of gumma.

An eminent member of the medical profession who had been unfortunately inoculated with syphilis died with hepatic cancer, which he had naturally at first hoped and believed to be gummatous disease.

Enlargement of the spleen from lardaceous or gummatous change is more likely to accompany syphilitic disease of the liver than malignant disease, and is a point to be borne in mind in diagnosis. When gummata are associated with lardaceous change in the same liver the enlargement may be very marked, and the resemblance to carcinoma very considerable. The irregularities produced by cicatrices in a lardaceous liver have a similar resemblance to malignant disease. In such cases albuminuria points to lardaceous disease, and therefore in favour of syphilis. Moreover, albuminuria is rare in malignant disease of the liver. In the following case adhesions over the surface of a lardaceous liver gave rise during life to a diagnosis of malignant disease:

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* Boix: Archiv. Général. de Med., June 2, 1903.

A man aged forty-one who had had a sore on the penis followed by a bubo, but who presented no other history or signs of syphilis or suppuration, was admitted to St. George's Hospital with ascites and albuminuria. After tapping nodules were felt over the surface of an enlarged liver and the tentative diagnosis of cirrhosis was given up in favour of malignant disease. At the autopsy the irregularities felt as nodules were due to peritoneal adhesions over the convexity of the liver; the liver weighed 9 pounds, was fatty and lardaceous, but presented no fibrosis, gummata, or new-growth. The spleen, 13 ounces, kidneys, suprarenal bodies, and intestines were lardaceous. One testis showed fibroid change in the body of the organ.

Difficulty sometimes arises in deciding between gummatous infiltration of a lobe of the liver and a hydatid cyst covered over by a layer of liver substance. The general health in hydatid is unaffected unless suppuration has occurred, and the liver is smooth, whereas in syphilis other signs of the disease and irregularity of the liver should be present. In any doubtful case iodides should be given at once. Gummatous and cicatricial deformity of the right lobe may produce a mass which imitates malignant disease of the gall-bladder.

IV. **Cases with Fever, Resembling Hepatic Suppuration.**—Occasionally irregular fever may occur in gummatous disease of the liver,* and may perhaps be explained as being due to secondary infection having occurred in gummata. The fever may suggest hepatic suppuration, malaria, latent tuberculosis, or even typhoid fever. It is, as a rule, removed by antisyphilitic treatment. When secondary infection takes place in a gumma, it may soften down and imitate an abscess. The association of a fluctuating swelling in the region of the liver and a raised temperature would render the resemblance to an ordinary hepatic abscess so close that unless the patient was known to have had syphilis there would be no reason to delay ordinary surgical treatment. A softened gumma may present anteriorly or may perforate through the ribs and project posteriorly or laterally. In a case operated upon by Newbolt † a softened gumma at the back of the right lobe was associated with and probably the cause of an empyema on the right side.

The abdomen of a woman aged twenty-six years, who had a well-marked syphilitic history, was opened during life, and a small gumma excised from the anterior margin of the liver. A hard mass was felt in the right lobe posteriorly and was thought to be a gumma. She was put on iodide of potassium and the right base was aspirated several times, but without success. At the autopsy there was an empyema on the right side and a suppurating gumma, apparently communicating with the empyema, in the posterior part of the right lobe of the liver.

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* Bristowe: Brit. Med. Journ., 1886, vol. i, p. 878. Gerhardt: Sem. Méd., June 22, 1898. Migliorato: Settim. Med., Nov. 26, 1898.

† Newbolt: Medical, Surgical, and Pathological Reports of Royal Southern Hosp., Liverpool, 1901, pp. 148. 248.

Tropical hepatitis around a previously quiescent gumma may imitate an abscess, and the true state of affairs be only revealed when caseous material instead of pus is removed at operation.

V. **Cases Resembling Gall-stones, etc.**—Jaundice is not really common in tertiary syphilitic disease of the liver, but occasionally the pressure of a gumma or the traction exerted by syphilitic cicatrices in the portal fissure may lead to obstructive jaundice. In rare cases this obstructive jaundice is accompanied by attacks of pain resembling biliary colic, but not due to the presence of gall-stones. The clinical aspects of such a case will closely resemble gall-stones. In any case of probable cholelithiasis with well-marked signs of tertiary syphilis iodides should be given before proceeding to operation. The following case recorded by Billings * bears on this point:

A single man aged thirty-seven who had contracted syphilis one and one-half years previously had constant pain in the region of the gall-bladder with attacks of colic followed by jaundice and accompanied by intermittent hepatic fever. A tumor was felt in the region of the gall-bladder and Finger operated for cholecystitis and calculi in the gall-bladder and cystic duct. Multiple gummata were found at the operation; the largest gumma was at the edge of the liver, close to the gall-bladder. The main ducts, however, did not appear to have been pressed upon, so the obstruction must have been in their branches. Finger had met with a similar case.

Gummata very seldom behave in such a way that they imitate a distended gall-bladder, as in the case just referred to and in another operated upon by R. Parker.† Such a case might naturally be thought to be one of impaction of a calculus in the cystic duct and secondary distension of the gall-bladder. In a case of suppurating gumma operated upon by Lilienthal ‡ the most probable diagnosis was cholecystitis.

VI. **Cases Resembling Chronic Splenic Anæmia.**—In some cases of syphilitic disease of the liver the spleen is greatly enlarged from lardaceous disease, or in rare instances from gummatous change, while the liver is little, if at all, enlarged. In such cases there may be a considerable resemblance to chronic splenic anæmia which is characterised by anæmia of the chlorotic type, leucopenia or a diminution in the number of leucocytes, and great splenic enlargement. In a case of Coupland's § the spleen was removed for supposed splenic anæmia with great apparent benefit. Subsequently the woman died from hæmatemesis and ascites and the liver was found to be syphilitic. Osler ‖ refers to similar examples of syphilis imitating chronic splenic anæmia in adults.

VII. **Cases Resembling Hypertrophic Biliary Cirrhosis.**—In rare instances syphilis may lead to an enlarged liver with chronic jaundice and splenic enlargement (Hanot**). There are signs of syphilis elsewhere in the body, the progress of the case is more rapid than in hypertrophic biliary cirrhosis, while the splenic enlargement is not so marked.

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* Billings: Philadelphia Med. Journ., 1900, p. 670.
† Parker, R.: Lancet, 1899, vol. i, p. 301.
‡ Lilienthal: Annals of Surgery, July, 1902, p. 132.
§ Coupland, S.: Brit. Med. Journ., 1896, vol. i, p. 1445.
‖ Osler, W.: American Journal of Medical Sciences, vol. cxxiv, p. 765, Nov., 1902.
** Hanot: Presse Médicale, Sept. 30, 1896, p. 505.

Lancereaux * assumes that Hanot was in error and that the condition was really leukæmia. A good example of syphilitic disease imitating hypertrophic biliary cirrhosis is given on page 324; the patient had tardive hereditary syphilis, chronic jaundice for years, enlarged liver and spleen, and clubbed fingers. Ferrannini described the case of a woman aged forty-eight years, with jaundice, clay-coloured stools, a large spleen and liver which resembled hypertrophic biliary cirrhosis. At the autopsy the enlargement of the liver and spleen were found to be due to syphilis and the jaundice to a retention cyst in the head of the pancreas compressing the common bile-duct.

DIAGNOSIS.

A history of syphilitic infection or the evidence of syphilitic lesions in some accessible part of the body, such as the skin, tongue, throat, testes, or bones, in an obscure case of hepatic enlargement or tumor, should always be regarded as an indication for antisyphilitic treatment. A patient may deny infection or may be entirely ignorant that he has contracted the disease.

In the following case the patient complained of hepatic pain, had an enlarged liver without jaundice or ascites, and denied syphilitic infection. A labourer aged fifty was under my care in St. George's Hospital in October, 1900. For a month he had constant pain in the right hypochondrium, worse at night when lying on the right side and on respiration. Married, no children, but his wife has had four miscarriages. The liver extends below the costal arch in the nipple line and is tender. Spleen not enlarged. Testes not enlarged. There is a rupial scar near the umbilicus. The tongue is greatly deformed and cannot be put out; it is scarred, shows superficial glossitis, and is lobulated, but not ulcerated. The tongue had been sore for six months and was ascribed by the patient to heavy smoking. On full doses of iodides and mercury the hepatic pain and the condition of the tongue rapidly improved. The case was one of gummatous disease of the tongue with probably a similar change in the liver.

Hepatic syphilis is probably very commonly overlooked, the disease being regarded as cirrhosis or early new-growth. It is therefore important to bear in mind the possibility of syphilis in all obscure enlargements of the liver and to give the patients the chance afforded by antisyphilitic treatment. Moreover, in doubtful cases invaluable assistance to diagnosis is obtained by watching the effects of a thorough course of mercurials and iodides. In the early stages of malignant disease it may be quite impossible to come to a correct decision until this has been tried. The differential diagnosis of syphilitic disease of the liver from cirrhosis, chronic peritonitis, malignant disease, etc., has already been referred to under the description of the clinical aspects of syphilitic disease of the liver.

PROGNOSIS.

When treated with sufficient doses of the iodides the prognosis is much better than in most of the conditions which resemble it, such as carcinoma, cirrhosis, chronic peritonitis, and perihepatitis. Gummata undergo absorption and the bad effects due to their mechanical effects will disappear. On the other hand, firm cicatrices will, as has already been pointed out, not be affected, and the results of antisyphilitic treatment are therefore disappointing, and, in addition, misleading if absence of a good result be regarded as necessarily eliminating syphilis. The

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* Lancereaux: Traité des Maladies du foie et du Pancreas, p. 513. 1897.

prognosis of syphilitic enlargement, which is often gummatous, is therefore rather better than that of ascites or jaundice thought to depend on syphilitic disease of the liver, since the latter may be due to cicatrices.

TREATMENT.

If syphilitic disease is suspected, mercurial inunction and iodide of potassium internally should be employed. Iodide of potassium should be combined with iodide of sodium and with an ammonia salt such as spiritus ammoniæ aromaticus. In this way the depressing effects of the potassium are avoided. The usual course is to begin with fifteen grains of the combined iodides three times daily, which is increased until 30 grains are being taken three times a day. If mercurial inunction be not employed at the same time, liquor hydrargyri perchloridi, ♏ xx, should be added to each dose of the medicine. The medicine should be taken shortly before meals. If taken after meals, dyspepsia may occur, probably because some free iodine is liberated by the action of the hydrochloric acid of the gastric juice on the iodides.

The use of iodide of potassium in tertiary syphilis appears to have been first discovered in 1831 by Dr. R. Williams, of St. Thomas' Hospital (Sir J. Paget*); though Dr. Wallace, of Dublin, who employed it in 1832 and published his results in the "Lancet" in 1836, is generally credited as the first to use this drug.†

It is important to remember that the good effects of iodides and mercury may take a considerable time to show themselves. It is essential, therefore, that several weeks' thorough treatment should be insisted upon before it can be concluded that the condition is not of a syphilitic nature.

An interesting speculation is opened up by a consideration of the marvellous way in which iodides produce absorption of gummatous material. This action can hardly be considered specific in the strict sense of the term, inasmuch as a similarly marked effect follows its adequate administration in actinomycosis. Possibly iodides act by preventing further disease of the vessels in the neighbourhood, and that this enables the natural process of absorption to go on unchecked by endarteritis of the neighbouring vessels, while it prevents any further manifestations of the syphilitic virus. Stockman‡ takes a different view, and believes that iodides act by bringing about increased secretion of the thyroid gland, which has a powerful absorptive action. If this be the case, thyroid extract should be given in gummata.

Flexner § attributes the absorption of gummata to autolysis or the action of intracellular ferments, and supposes that this ferment action is accelerated by iodides.

If the patient is anæmic, iron should be given and iodide of iron is a convenient form. When gummata develop with great rapidity and soon after infection, subcutaneous, or better intramuscular, injection of mercurial salts may be employed. The benzoate of mercury, which is soluble, has been used with advantage.

Pain due to perihepatitis may be relieved by hot fomentations, by

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[*] Sir James Paget: Address to the Abernethian Society of St. Bartholomew's Hospital, 1885, p. 19. Privately printed. Quoted by Howard Marsh in obituary notice of Sir J. Paget, St. Bartholomew's Hospital Reports, vol. xxxvi, p. 6.

[†] See Lancereaux: Syphilis, vol. ii, p. 300. In New Sydenham Society's Library.

[‡] Stockman: Glasgow Hospital Reports, 1899, p. 69.

[§] Am. Jour. Med. Sc., vol. cxxvi.

poultices, or by the application of a few leeches over the painful area. The general health should be maintained by a generous diet and by fresh air, preferably that of the sea. In severe cases with cachexia the medicinal treatment may with advantage be carried out at spas of high elevation; Sir Hermann and Dr. Parkes Weber recommend Barèges, Cauterets, Bagnères-de-Luchon, or Wildbad-Gastein. Aix-la-Chapelle and Wiesbaden are well adapted for the treatment of visceral syphilis.

The surgical treatment of gummata of the liver by removal may be possible when the anterior margin of the liver is affected, and when the lesion is single and localised, but it is only likely to be performed in cases where an exploratory operation has been undertaken for purposes of diagnosis and where a tumor of uncertain nature is found and can be fairly easily removed. In exceptional instances when a breaking-down gumma is ulcerating through the abdominal wall, scraping out the gummatous sloughs, as in a case described by W. G. Spencer,* is advisable, inasmuch as septic absorption is thus prevented.

In a case where an exploratory operation revealed a very large gumma 4 or 5 inches across, R. Parker† removed some, but not all, of the caseous contents and then closed the wound; antisyphilitic remedies were afterwards given and the man recovered.

Removal of a localised gumma or of a gummatous constriction lobe in cases where laparotomy has been undertaken to clear up the diagnosis, or under the impression that some other condition was present, is admissible, inasmuch as it may accelerate the cure by antisyphilitic treatment. But a very thorough course of antisyphilitic treatment should be carried out before an operation is undertaken with the view of removing a gumma.

Keen ‡ in 1899 collected twelve cases where resection of the liver had been performed for gumma, and in 1903 Cumston § brought the number up to twenty-seven. In most cases operation was undertaken under the idea that the hepatic condition was other than a gumma. Steiner ‖ has collected thirteen cases in which laparotomy was planned on what turned out to be errors of diagnosis.

PARASYPHILITIC AFFECTIONS.

By parasyphilitic or metasyphilitic lesions are meant changes which are not in their nature pathognomonic of syphilis, but which develop when the soil has been prepared by the poison of syphilis, such as tabes dorsalis and general paralysis of the insane. The question of parasyphilitic multilobular cirrhosis occurring in the subjects of congenital syphilis is discussed elsewhere. Pathologists have insisted, and rightly, on the difference between ordinary alcoholic cirrhosis and the specific forms of hepatic fibrosis—namely, pericellular cirrhosis in hereditary syphilis and multiple scarring by cicatrices. This may account for the fact that little attention has been paid to the question whether a parasyphilitic multilobular cirrhosis need be recognised as a sequela of syphilis. That it not uncommonly happens that a person who has had syphilis becomes the subject of ordinary multilobular cirrhosis is quite natural, since syphilis does not protect in any way against the effects of alcoholism, and, moreover, Bacchus and Venus are frequently worshiped by the same devotees. It is reasonable to believe that parasyphilitic multilobular cirrhosis may occur in adults, but there are considerable difficulties in recognising it or in establishing its existence.

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* Spencer, W. G.: Brit. Med. Journal, 1898, vol. ii, p. 1686; and Trans. Clin. Soc., vol. xxxii, p. 46.

† Rushton Parker: Lancet, 1899, vol. i, p. 301.

‡ Keen, W. W.: Annals of Surgery, Sept., 1899, p. 267.

§ Cumston, C. G.: (Boston, U. S. A.) Archiv. Général. de Méd., t. 191.

‖ Steiner: Thèse Paris, 1902. No. 380, p. 897, 1903.

Lardaceous Disease.—With the advance of antiseptic surgery prolonged suppuration is so much less common than formerly that syphilis is responsible for a much larger proportion of cases of lardaceous disease than formerly. Lardaceous liver is considered elsewhere; it need only be stated here that lardaceous change may accompany gummatous and other syphilitic lesions in the liver and that in some instances the lardaceous change is limited around gummata.

CONGENITAL SYPHILIS OF THE LIVER.

The hepatic lesions due to congenital or hereditary syphilis may conveniently be considered as: (1) Those found in infants at the same time that other manifestations of congenital syphilis are present. (2) Those of delayed or tardive congenital syphilis. (3) Multilobular cirrhosis supervening in children with a history or signs of former hereditary syphilis, or parasyphilitic cirrhosis.

The first of these categories is far the most important and contains the account of what is ordinarily understood by the liver of congenital syphilis.

History.—Gubler * first gave a full description of the lesions of the liver in hereditary or congenital syphilis in 1852. Bamburger, Virchow, and Parrot further described the condition, while in Great Britain Sir S. Wilks recorded a case in 1866. The reader will find references to the history of hereditary hepatic syphilis in Lancereaux's † work on syphilis. More recently the tertiary effects of congenital syphilis on the liver have been specially described in cases of syphilis hereditaria tardiva.

THE ORDINARY HEPATIC MANIFESTATION OF CONGENITAL SYPHILIS.

Incidence.—The liver is found to be affected in a very high proportion of the infants dying with congenital syphilis.

In infants with congenital syphilis the liver has been found to be affected in from 39 per cent. (Hofmeister ‡) to 65 per cent. (Feige §).

This contrasts with acquired syphilis, in which the liver very frequently escapes. It is generally considered that antenatal syphilis may be either (I) hereditary, and due to the spermatozoön being the carrier of the syphilitic germ or poison to the ovum, while the mother escapes though rendered immune to further infection; or (II) congenital, and due to the syphilitic toxine passing from the mother through the placenta into the umbilical vein of the fœtus. The frequency of hepatic lesions in congenital syphilis is an argument in favour of the view that antenatal syphilis is maternal, the infection passing through the placenta into the umbilical vein and damaging the liver, which is the first organ of the fœtus with which it comes in contact; while if the ovum were primarily infected by a syphilised spermatozoön it is improbable that the embryo would survive; and further, if it did, the syphilitic toxine would reach the liver by the hepatic artery, and the liver, being thus exposed to the same risk of infection as in postnatal syphilis, should be affected in much the same proportion as in the acquired disease. In postnatal syphilis when the disease is conveyed by suckling from a wet-nurse, by inoculation, or other means, the lesions are the same as those of acquired syphilis.

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* Gubler: Soc. de biolog., tome iv, p. 25, 1852.

† Lancereaux: Syphilis, vol. ii, pp. 132, 151. Transl. New Sydenham Soc.

‡ Hofmeister: Dissertation, Kiel, 1886. Quoted by Quincke in Nothnagel's Encyclopædia of Practical Medicine, English translation, p. 745.

§ Feige: Dissertation, Kiel, 1896. Ibid.

Morbid Anatomy.—*Liver.*—There is very considerable variation in the changes found in the livers of infants dying with congenital syphilis; but the two main points in regard to the morbid anatomy are, (I) that the change tends to be diffuse, and (II) that it is a secondary syphilitic manifestation. Congenital hepatic syphilis thus differs markedly from the circumscribed lesions of the liver characteristic of the tertiary stage of the acquired disease. The appearance of the liver is by no means constant; there is sometimes little or no manifest change to the naked eye, and microscopic examination alone may make it certain that there is syphilitic infection. The liver is enlarged, usually retains its shape, and weighs more than natural, being one-twelfth or one-sixteenth instead of one-twenty-fifth of the body-weight at birth. The surface may show adhesions, due to intrauterine perihepatitis and peritonitis, but except for these adhesions the liver is smooth, and is firmer and more resistant than normal. The healthy colour is altered; occasionally, in the early stages of the disease, it is congested, but usually its tint is lighter than in health; it may be violet, greyish-yellow, and approaching the colour of flint (*Foie Silex* of Gubler) or yellow. On section it is firmer than natural and resistant, but not to the same extent as in cirrhosis or in congenital obliteration of the bile-ducts. The organ tends to be uniformly affected, but often some parts are more affected than others, so that a marked or mottled appearance is presented. The alteration in colour is the same as described above, but the mottling may be more marked; areas presenting the yellow change may alternate with parts preserving the more or less healthy red colour, and the appearance may suggest primary sarcoma. In other instances the glistening, semi-translucent aspect resembles that of a lardaceous liver.

On carefully examining the cut surface small grey spots like grains of semolina are generally visible; they are small granulomata or syphilomata, and, though not caseous, are often spoken of as miliary gummata. The left lobe is said to be more often affected with these syphilomata.

To the naked eye these look like small miliary tubercles, and microscopically they so far resemble them in being localised collections of small round cells. Tubercle may indeed be associated with intercellular cirrhosis, and the distinction between these small syphilomata and miliary tubercles depends on the absence of tubercle bacilli. In rare instances definite caseous gummata have been found in infants and even in still-born children and premature fœtuses.

Canton * has figured multiple hepatic gummata in a child of seven weeks, and Sir T. Barlow † gave a description of "receding gummata" in a child twelve weeks old. Bittner ‡ has recorded gummata in the liver of a still-born child and in a six months' fœtus. A number of other cases are given by Lancereaux § and by Hutinel and Hudelo. ‖

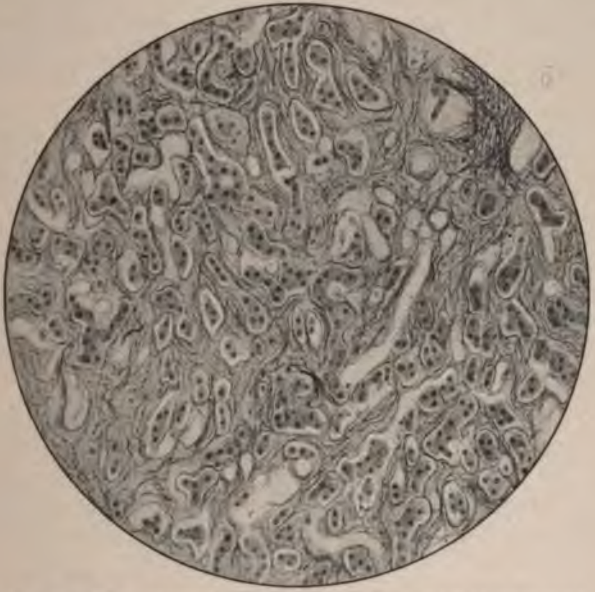

FIG. 45.—MICROSCOPIC APPEARANCES IN PERICELLULAR CIRRHOSIS. There is delicate connective tissue between the small groups of liver cells.

The microscopic appearances vary very greatly according to the duration and virulence of the infection. In the earliest stage there is capillary congestion with commencing small-cell infiltration, which subsequently becomes diffuse, spreads widely between the liver cells, and may invade the portal spaces. These newly formed cells are the outcome of proliferation of (*a*) the pre-existing connective-tissue cells of the organ; (*b*) of the endothelium of the capillaries and lymphatics inside the hepatic lobules, while Kupffer's star-like cells, which are intimately connected with the endothelial lining of these vessels, share in this process. This diffuse infiltration closely resembles an infiltrating sarcoma, and naturally, since proliferation of the connective tissues during fœtal life or soon after birth leads to a formation which is structurally much the same as that of a sarcoma. It is extremely probable that some cases described as diffuse sarcoma in early life were in reality examples of the hepatic lesion of hereditary syphilis.

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* Canton, E.: Trans. Path. Soc., vol. xiii, p. 113.

† Barlow, T.: Ibid., xxvii, p. 202.

‡ Bittner: Prag. med. Wochen., Bd. xviii, S. 581. 1893.

§ Lancereaux: A Treatise on Syphilis, vol. ii, p. 152. Translat. New Sydenham Soc., 1869.

‖ Hutinel and Hudelo: Archiv de Méd. expériment. et d'Anat. path., p. 509, tome x, 1890.

At a rather later stage the infiltrating cells have become elongated and as fibroblasts separate the individual liver cells from each other. There is thus a pericellular, unicellular, or monocellular cirrhosis. This appearance is occasionally seen in the secondary stage of syphilis, and locally in some cases of ordinary portal cirrhosis. Sometimes the microscopic appearances of pericellular cirrhosis at this stage are like those of an infiltrating carcinoma, the liver cells representing the epithelial cells of carcinoma and the cirrhosis the alveolar walls.

It is interesting to note that Adami * described pericellular cirrhosis in the Pictou cattle disease of Nova Scotia. The change is due to a minute diplo-bacillus, and gives rise, unlike congenital syphilitic disease of the liver, to ascites, diarrhœa, and muscular weakness—in short, to symptoms like those of ordinary cirrhosis.

As time goes on the organisation of young connective tissue may advance and lead to well-formed fibrous tissue. The chronic nature of the inflammation, if allowed to run its course, is often well shown by the presence of both well-formed fibrous tissue and recent inflammatory or granulation tissue in the same specimen. The fibrous tissue of Glisson's capsule in the portal canals is also increased in amount. In places there may be collections of small round cells—syphilomata—or, as they are often called, miliary gummata, though the word "gumma" should be reserved for the further stage, where necrosis and caseation have supervened. These small syphilomata may be found in association with early pericellular infiltration, or later, when there is well-formed fibrous tissue.

The hepatic lesions which can be regarded as a remote result of congenital syphilis will be referred to again under the heading of Delayed Congenital Syphilis, but here it may be pointed out that although ordinary cirrhosis may very probably supervene in a liver recovering from pericellular cirrhosis, it does not appear reasonable to imagine that pericellular cirrhosis can be directly transformed into multilobular or monolobular cirrhosis. Very marked fibrosis attacking large areas of the liver and producing a tumor-like mass is a change sometimes seen as the result of congenital syphilis. Some cases of the kind have been described as fibroma of the liver. Marchand † has insisted on the syphilitic nature of these cases.

As an example of very extensive fibrosis Morley Fletcher's ‡ case of a child aged eight weeks may be referred to. The mother had had seven other healthy

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* Adami, J. G.: Middleton-Goldsmith Lecture, 1896.

† Marchand: Centralblatt f. allg. Path., Bd. vii, S. 273, 1896.

‡ Morley Fletcher, H.: Trans. Path. Soc., London, vol. l, p. 138.

children and one still-born infant, but no other evidence of syphilis was forthcoming. The liver was much enlarged and easily felt. There was no jaundice or ascites. The liver weighed 28 ounces and microscopically showed great fibrosis, the fibrous tissue being well formed; in addition, there were areas with much small-cell infiltration. The hepatic cells were greatly atrophied, compressed, and in many places formed columns resembling pseudo-bile canaliculi (*vide* Fig. 46); there was a considerable amount of extravasation of red corpuscles. The spleen was not enlarged. The right suprarenal was enlarged to the size of its corresponding kidney and there were fibrosis and extravasation into the medulla. In this case, as in those recorded by Marchand, some doubt as to the existence of syphilis might arise.

The liver cells are atrophied and compressed as if from pressure, and may show granular and degenerative changes. Fatty change is not frequent, and when present is usually quite sporadic and localised. As the result of necrosis they may disappear from considerable areas, their place being taken by organising granulation tissue. The liver cells may be so compressed that they closely resemble newly formed bile-ducts. This may be explained in two ways: (*a*) on the supposition that the specific changes began early in fœtal life and arrested the development of the liver parenchyma so that it remained in many parts as a tubular gland, while in other areas the liver cells, being less interfered with, were able to develop more or less normally; (*b*) on the hypothesis that these pseudo-bile canaliculi are an attempt at compensation by hyperplasia of the remaining liver cells.

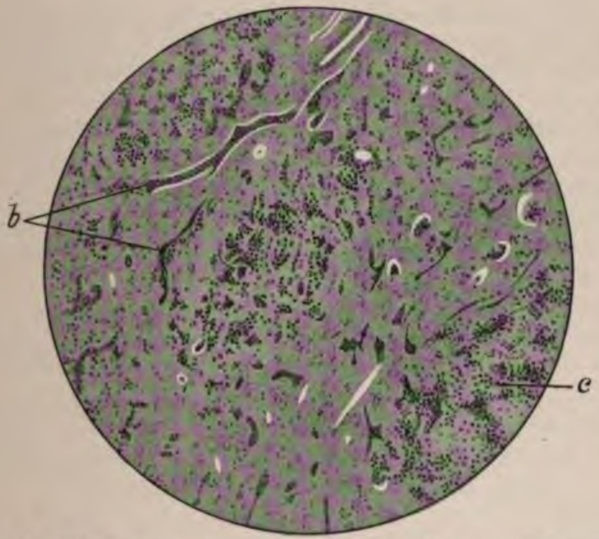

FIG. 46.—MICROSCOPIC SECTION FROM A CASE OF CONGENITAL SYPHILIS.
Showing extensive fibrosis, areas of small-cell infiltration (*c*), compressed liver cells, and columns of cells resembling small bile-ducts (*b*). (Drawing kindly lent by Dr. H. Morley Fletcher.)

Adami * regards the changes in the liver cells as primary, and due to the action of the poison, and the pericellular infiltration as secondary and of the nature of a replacement fibrosis. The view which appeals more to my mind is that both the degenerative changes in the liver cells and the pericellular cirrhosis are concomitant results of the same factor—the poison.

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* Adami, J. G.: New York Med. Journ., April 22, 1899.

The hepatic artery is normal and is free from endarteritis, a change which would naturally be expected if the syphilitic virus reached the liver from the general circulation. In exceptional instances, however, endarteritis and peri-arteritis and phlebitis are present. (Obernderfer.*) There is an increase in the amount of fibrous tissue and in exceptional instances marked inflammatory changes around the bile-ducts and portal vein in the portal spaces. Endophlebitis of the branches of the hepatic veins sometimes occurs, and if allowed to progress, may eventually lead to stenosis of the orifice of these veins. (*Vide* p. 50.)

The variations met with in the liver in congenital syphilis depend on the severity of the infection and its duration. The following conditions may be recognised:

I. The commonest change is a diffuse embryonic infiltration which subsequently develops into young connective-tissue cells separating the individual liver cells; this is pericellular, unicellular, or monocellular cirrhosis.

II. The previous condition may be combined with small collections of round cells or miliary gummata.

III. Further organisation of the pericellular infiltration leads to widespread or local areas of fibrosis.

IV. Occasionally well-formed caseous gummata like those seen in adults are present.

V. A combination of gummata with fibrosis (gummatous hepatitis) not affecting the whole organ, but forming circumscribed areas which occasionally may be so marked as to imitate a new-growth or tumor.

The diffuse monocellular cirrhosis is, like the lesions of secondary syphilis elsewhere in the body, an essentially curable condition if treated with mercury. It may, however, pass into the tertiary lesions, and gummata, cicatrices, and lardaceous changes may develop. (*Vide* Delayed Congenital Syphilis, p. 375.)

The spleen is generally enlarged, and from fibrosis becomes firmer than natural. Lardaceous disease may be seen in older children. Gummata are extremely rare; Still † could only find two cases in infants. There may be adhesions between the capsule and adjacent parts. Microscopically there is fibrosis.

The kidneys may also present interstitial fibrosis.‡ This is a point of interest in connexion with Payne's § view that granular kidneys in young children depend on hereditary syphilis. There may be diffuse small-cell infiltration in the pancreas and testes, while changes in the lungs are comparatively frequent. The suprarenal bodies are larger than natural. There may be small-cell infiltration, hæmorrhage, or fatty change.

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* Obernderfer: Centralblattf. allg. Path. u. path. Anat., March 25, 1900.
† Still: Trans. Path. Soc., vol. xlviii, p. 205.
‡ Hebb, R. G.: Trans. Path. Soc., vol. xlviii, p. 117.
§ Payne, J. F.: Ibid., vol. li, p. 364.

Clinical Features.—When the infection is advanced, the child may be still-born or die a few days after birth. In many cases the child is healthy when born and subsequently develops evidences of congenital syphilis. As a general rule, signs pointing definitely to the liver, such as jaundice and ascites, are absent, and it is only on examination that the liver and spleen are found to be enlarged. The clinical features may be summarised in a word. The well-known manifestations of hereditary syphilis are present, and, in addition, there is evidence of enlargement of the spleen and liver.

The liver is enlarged: it may even reach down to the iliac crest. This enlargement is frequent in congenital syphilis; in 148 cases it was palpably so in 48. (Hochsinger.*) In connexion with the enlargement of the liver it must be borne in mind that normally in young children the liver projects further down than in adults; this, Henoch points out, is not merely due to the relatively larger size of the organ in children, but also to the ribs being more horizontal and so leaving the organ more uncovered. Hence slight apparent enlargement must not be regarded as of any importance in the absence of other evidence. The degree of hepatic enlargement corresponds with that of the other manifestations of the disease, and may therefore be taken as an index of the severity of the infection.

The liver is firm, tender, and somewhat resistant. In some cases there is a localised tumor formation which is readily felt during life. These cases are, of course, very rare; reference to Marchand's cases has already been made.

In a child three months old, icterus, ascites, and cerebral symptoms were associated with a gummatous growth projecting from the under surface of the right lobe of the liver. (Cohn.†)

The spleen is enlarged in cases of hereditary syphilis. This universally accepted fact was pointed out by Gee ‡ in 1867, who found clinical evidence of splenic enlargement in one-fourth of the cases of hereditary syphilis.

More recently the incidence of splenic enlargement in congenital syphilis has been estimated at 45 per cent. by Still,§ and at 63 by Coutts.‖

Jaundice occasionally occurs, and is probably not so extremely rare as is often stated. It may be explained as due to various factors. It may possibly depend on pressure of enlarged glands in the portal fissure on the ducts, or on pressure exerted by masses of syphilitic granulation tissue, but is more probably due to inflammatory changes in the small bile-ducts which form part of the diffuse pericellular hepatitis. In the latter case it is much the same as the jaundice occasionally seen in the secondary stage of acquired syphilis. Milon ** has drawn attention to secondary infection as a cause of jaundice in congenital syphilis; in two of his cases the infective agent was Proteus vulgaris and the colon bacillus respectively. The micro-organisms may enter through the umbilical vein and find a suitable nidus in the liver, the resistance of which has been reduced by the syphilitic lesion. The development of jaundice is thus comparable to icterus gravis supervening in ordinary cirrhosis. The aspect of the case may then be one of multiple hæmorrhages and resemble the acute umbilical infections in the newly born. Perry and Shaw * refer to a case of this kind, which was regarded as primarily syphilitic, in an infant two weeks old.

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* Hochsinger: Wiener med. Wochen., Bd. xlvi, S. 345, 1896.
† Cohn, M.: Virchow's Archiv, Bd. cxlvi, S. 468.
‡ Gee, S.: Brit. Med. Journ., 1867, vol. i, p. 435.
§ Practitioner, vol. lxxiii, p. 101.
‖ Brit. Med. Jour., 1896, vol. i, p. 1025.
** Milon: Thèse Paris, 1897, No. 434.

When jaundice is met with in congenital syphilis, it is usually present at birth, but it may not come on until some weeks later. In rare cases the jaundice may be seen to pass away and return again.

Still † refers to a boy who was jaundiced for the first six weeks of life; he then recovered and appeared perfectly healthy until the age of two years and three months, when he again became attacked by jaundice, which, after lasting some weeks, proved fatal. Microscopically the liver showed intercellular cirrhosis.

Ascites in like manner is very rare; it may be due to concomitant peritonitis and perihepatitis, which are not very rare in severe cases of the disease; or possibly to the pressure of enlarged glands in the portal fissure. In intrauterine life hepatic syphilis may so interfere with the circulation through the umbilical vein as to produce hydramnios, and a number of premature deaths are thus accounted for. But in infants which survive there is not sufficient phlebitis of the portal vein to produce ascites. The abdomen is somewhat distended, partly from enlargement of the liver and spleen, and partly from tympanites. As already pointed out, ascites is very rarely present. Prominence of the subcutaneous abdominal veins is sometimes noticeable. The usual symptoms and signs of congenital syphilis, such as debility, wasting, the cutaneous, mucous, and bony lesions, anæmia, and in some cases multiple hæmorrhages, vomiting, and diarrhœa, are present.

Diagnosis.—This is usually very much easier than in acquired syphilitic disease of the liver in adults, inasmuch as there are usually well-marked signs of syphilis elsewhere in the body of the infant. In the absence of these signs other causes for enlargement of the liver and spleen, such as rickets, tuberculosis, gastro-intestinal infection, and the various forms of anæmia, must be considered and as far as possible eliminated. In cases where there is jaundice from birth without any manifest signs of syphilis simple catarrhal jaundice and congenital obliteration of the ducts must be borne in mind. In cases of doubt much assistance will be obtained by a course of mercurial treatment.

Prognosis.—The prognosis depends on the general state of nutrition and on efficient and prompt anti-syphilitic treatment. If the liver and spleen are greatly enlarged, the prognosis is grave. Visceral enlargement may be regarded as an index of the severity of the infection. The occurrence of hæmorrhages is of bad omen, and cases with jaundice usually do badly.

* Perry and Shaw: Guy's Hosp. Reports, vol. l, p. 226.

† Still: Clinical Journal, vol. xvii, p. 322, 1901.

Treatment.—The treatment is that of congenital syphilis with mercury by inunction or by the mouth. Hydrargyrum cum cretâ may be given in the form of a powder: to a child under two months $\frac{1}{2}$ grain twice a day; after that age the dose being increased to one grain. Liquor hydrargyri perchloridi may be given instead or the French preparation of Liqueur de Van Swieton in doses of 10 minims daily for a child of one month old, increasing the doses by 5 or 10 minims every month or so. A more satisfactory method, both because it acts more rapidly and is less likely to lead to salivation, is mercurial inunction. Mercurial ointment is rubbed on with flannel, into the axillæ, over the liver, and over the spleen, a fresh situation being selected daily. To begin with, about 15 grains of the ointment should be used every day.

The mercurial treatment should be carried out daily for three months, and then relaxed gradually; in the fourth month the treatment being intermitted for a week at a time, and in the fifth month for two weeks. In the second year of treatment mercurial inunction should be performed during one month out of three, and small doses of iodide of potassium given. In the third year the dose of the iodide may be increased, and in the fourth year the mercurial treatment may be dropped, while the iodide is continued. In this way the appearance of tertiary manifestations should be prevented. As a means of preventing both abortion and syphilitic infection of the fœtus a pregnant woman known to be the subject of syphilis should go through a course of anti-syphilitic treatment.

THE HEPATIC MANIFESTATION OF DELAYED CONGENITAL SYPHILIS.

Synonym: Tardive Hereditary Syphilis.

Description.—The changes in the liver are the same as in the tertiary stage of the acquired disease, but they occur in the subjects of undoubted hereditary or congenital syphilis.

History.—The recognition of this form of syphilis is usually credited to Fournier in 1886. Probably the earliest recorded case was described in 1863 by Sir S. Wilks;[*] the patient was a girl aged twelve years whose mother had had secondary syphilis. The child's liver was much deformed and contained gummata and numerous cicatrices.

H. Morris'[†] case is worth referring to as one of the earlier examples of tardive hereditary syphilis. The patient was a girl aged twenty years with a family history of syphilis and a personal history of interstitial keratitis. The liver was noticed to be enlarged at eighteen and ascites appeared in the course of the next year. At the autopsy the liver, which weighed thirty-nine ounces, was fissured, puckered. lardaceous, and contained gummata; the kidneys and spleen were also lardaceous,

Incidence.—The disease is not very rare. In 1885 Fournier[‡] collected 25, and in 1890 Hudelo[§] referred to 49, cases. In 1902 Forbes[‖] collected 132 cases showing the lesions of late hereditary syphilis in one form or another. In 34 per cent. of Forbes' cases the liver was affected with changes other than lardaceous disease, such as cicatrices, gummata, cirrhosis, or perihepatitis. It may come on in any of the first three decades of life or even later; more than half occur in the second decade.

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[*] Wilks, S.: Guy's Hosp. Rep., 1863.

[†] Morris, H.: Trans. Path. Soc., vol. xxi, p. 214.

[‡] Fournier: La Syphilis hereditaire tardive, 1886.

[§] Hudelo: Quoted by Chauffard, Traité de Médécine [Bouchard, Brissaud], tome v, p. 265.

[‖] Forbes: St. Bartholomew's Hosp. Reports, vol. xxxviii, p. 37.

In Forbes' cases 26.5 per cent. came on in the first decade, 57.5 in the second, 12.3 in the third, and 3.7 in the fourth.

The presence of gummata in the livers of infants or in exceptional instances in new-born children shows that the same changes may occur very early in life. The hepatic lesions are tertiary in character and exactly resemble those seen in the acquired disease. The secondary lesions having persisted, and instead of being cured by treatment have been succeeded by the tertiary lesions commonly present in acquired hepatic syphilis and sometimes seen in the early stage of the hereditary disease. Tardive congenital syphilitic disease of the liver therefore forms a connecting link between the ordinary congenital and acquired types of hepatic syphilis. In order to be sure that the case is one of delayed congenital syphilis there must be some other evidence of the congenital affection, such as interstitial keratitis, otherwise the disease might have been acquired in early life; for example, from a wet-nurse.

Morbid Anatomy.—The liver is nearly always enlarged and is changed in much the same way as in the tertiary stage of the acquired disease. It may be very greatly deformed and cut up into numerous lobes; it is highly probable that some of the recorded anatomical abnormalities of multiple lobulation (as many as 16 lobes have been described) can be thus explained. The lesions are gummata, cicatrices, fibrosis, pericellular cirrhosis, and lardaceous change in varying degrees and combinations. (*Vide* Lesions of the Liver in Acquired Syphilis.) It is well to remember that, as in early congenital syphilis, the naked-eye appearance of the liver may suggest malignant disease; this was the first naked-eye diagnosis in a boy aged fifteen years with tardive hereditary hepatic syphilis described by H. W. G. Mackenzie.* Perihepatitis is common and may be the means by which gummatous inflammation spreads to the abdominal wall. The other organs may show syphilitic lesions and advanced lardaceous disease.

Clinical Features.—The subjects of tardive hereditary syphilis usually display copious signs of syphilitic infection in the bones, sense organs, or in the existence of widespread lardaceous disease. They are ill developed, look much less than their years, and are examples of what has been called infantilism. The liver is nearly always enlarged and may even appear as a tumor; this point is illustrated in cases recorded by Post † and Bristowe.‡

In Post's case, a boy aged twenty-two years, the subject of late hereditary syphilis, there were gummata in various bones, in the pancreas, and in the liver. A gumma in the liver had become adherent to and invaded the abdominal wall, giving rise during life to a very definite tumor. Besides gummata the liver showed very diffuse fibrosis. As is not uncommonly seen in severe examples of syphilis, the patient died from an acute secondary infection with streptococci. Bristowe's case, a boy aged fifteen years, had a tumor of uncertain nature connected with the liver which yielded nothing on aspiration. The temperature was hectic. As there was reason to believe that the boy was the subject of congenital syphilis, anti-syphilitic remedies were employed and the signs and symptoms all disappeared.

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* MacKenzie, H. W. G.: Trans. Path. Soc., vol. xliii, p. 84.
† Post: Boston City Hospital Reports, 1898, p. 233.
‡ Bristowe: Brit. Med. Journ., 1886, vol. i, p. 878.

The spleen is enlarged either from lardaceous change or independently, as in the following case,* which imitated hypertrophic biliary cirrhosis.

A boy aged seventeen years, under the care of my colleague, Dr. Ewart, had chronic jaundice of some years' duration, subcutaneous gummata, periostitis, enlargement of the spleen and liver, and clubbed fingers. He was the subject of congenital syphilis. Death was due to erysipelas complicated by pericarditis and peritonitis. The liver weighed 5 pounds, the right lobe was much scarred by gummata and was small, a fibrous mass compressed the common hepatic duct just at its commencement and obstructed the entrance of the two hepatic ducts into it. The spleen weighed 45 ounces. None of the organs were lardaceous.

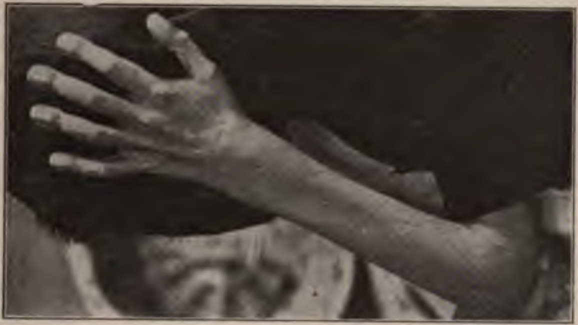

FIG. 47.—PHOTOGRAPH SHOWING CLUBBING OF FINGERS IN A CASE OF TARDIVE HEREDITARY SYPHILIS. (Photographed by Dr. H. G. Drake Brockman.)

There may be œdema of the feet and evidence of lardaceous disease of the kidneys, and eventually uræmia. Jaundice is rare, while ascites is very common. Jaundice and ascites may be due to pressure exerted by gummata or cicatrices in the portal fissure, while ascites may be part of the general dropsy of lardaceous kidney disease. In some instances there is widespread arteriosclerosis, with so much narrowing of the arteries (endarteritis obliterans) that the pulses in the limbs may be absent. Death may be due to secondary infections, such as erysipelas, or be due to uræmia, cardiac failure, or asthenia.

Diagnosis.—The diagnosis rests on the evidence of congenital syphilis, as shown by interstitial keratitis, Hutchinson's teeth, deafness, and infantilism, together with hepatic enlargement. If evidences of syphilis common to the congenital and the acquired forms, such as gummata and lardaceous disease, are present and none of the stigmata of the congenital variety are obvious, the infection may have been acquired in early life. But from the point of view of treatment an accurate distinction between tardive congenital and ordinary syphilitic disease of the liver is unnecessary.

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* Lazarus-Barlow, W. S.: Trans. Path. Soc vol. l, p. 158.

The following case illustrates the difficulties which may arise in classification: there was tardive hereditary syphilis, but the hepatic lesions were of the secondary and not of the tertiary stage. Clinically the hepatic enlargement must have appeared to have been undoubtedly of a tertiary nature.

In a marked case of the congenital syphilitic disease with Parrot's pseudoparalysis, deafness, and other stigmata in a girl aged twenty-one years, recorded by Touche,* the liver, which weighed 104 ounces, only showed pericellular cirrhosis, although gummata and tertiary lesions were present in the bones.

When, as is often the case, the most prominent features are those of enlarged liver, ascites, and lardaceous disease, the diagnosis turns on evidence of past syphilis; failing this and any other cause for lardaceous disease, such as prolonged suppuration, the possibility of tardive hereditary syphilis should be thought of.

Prognosis.—The prognosis is not so favourable as in acquired tertiary syphilis of the liver; the effects of the poison are more widespread, and the frequency with which extensive lardaceous disease is present makes the outlook very grave. The *treatment* is that of acquired syphilis in its tertiary stage. (*Vide* p. 365.)

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Touche: Bull. Soc. Anat. Paris, 1900, p. 852.
Tzeytline: Thèse Paris, 1896.
Wilks: Guy's Hosp. Reports, vol. ix, p. 24, 1863.
Wills: Liverpool Medico-Chirurg. Journ., July, 1892.

PARASYPHILITIC MULTILOBULAR CIRRHOSIS.

The subsequent development of multilobular cirrhosis in young persons the subjects of congenital syphilis is a point of considerable interest. The diffuse pericellular cirrhosis of infants suffering from congenital syphilis is, like the lesions of the secondary stage of the acquired disease, a curable condition. Microscopic examination of the livers of children formerly affected with well-marked hereditary syphilis may show no disease. On the other hand, every now and again the liver of a child who bears undoubted stigmata of congenital syphilis in the body is found to show ordinary cirrhosis. The arrangement of the two lesions is so dissimilar that pericellular cirrhosis cannot be thought to be transformed into multilobular cirrhosis; it would rather lead to diffuse fibrosis or gummatous change. It seems probable that the pericellular cirrhosis undergoes absorption, but that some vulnerability or diminished resistance of the liver is left behind. If causes then arise that tend to produce ordinary cirrhosis, this change will be readily produced. In other words, the multilobular cirrhosis is a parasyphilitic lesion, and is comparable to general paralysis of the insane, in that though not syphilitic, it is favoured by syphilisation of the soil.

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* Touche: Bull. Soc. Anat. Paris, 1900, p. 852.

Sometimes multilobular cirrhosis due to its ordinary causes may supervene in a liver where pericellular cirrhosis still exists. This would account for some cases of very extensive fibrosis, chiefly of the multilobular type, but where there are in addition areas of fibrosis suggesting that pericellular cirrhosis has gone on to organisation. Occasionally in multilobular cirrhosis occurring early in life in the subjects of congenital syphilis there is early lardaceous change in the organ.

The **clinical features** of these cases of ordinary cirrhosis supervening in the subjects of congenital syphilis are much the same as those of portal cirrhosis in children, viz., portal obstruction, ascites, wasting, etc. In some instances it will be difficult to distinguish between the cases of cirrhosis with facial and other stigmata of hereditary disease and cases of tardive hereditary syphilis with ascites; in the latter disease there may be lardaceous disease of the various organs, including the kidney, as shown by albuminuria. What proportion of the cases of advanced portal cirrhosis of the liver in children have a syphilitic substratum it is difficult to say with certainty; but the statistics of reported cases make it clear that direct evidence of syphilis is often absent. The following case illustrates the very marked degree of cirrhosis that may develop in the wake of congenital syphilis and the importance of a careful microscopic examination in distinguishing this condition from tardive hereditary syphilis:

A boy aged thirteen years, who had never taken alcohol, was the third child of his mother, who had four miscarriages, all after his birth. In May, 1898, the abdomen enlarged, he became languid and tired, and in August he became short of breath, and hæmatemesis and melæna occurred. When admitted to St. George's Hospital under the care of Dr. Penrose, the liver was found to be much enlarged, reaching three fingerbreadths below the costal arch, and dilated veins were present on the abdominal wall. Ascites developed and he was twice tapped; death occurred three weeks after the last tapping. There was no œdema of the feet or albuminuria. At the autopsy the liver, 42 ounces, was enlarged and granular on the surface; on section there were white areas suggesting gummatous infiltration. These were especially well marked around the hepatic veins, and by narrowing them had induced thrombosis. Microscopically, however, these areas showed no caseation, while there was a high degree of fibrosis, multilobular and intercellular cirrhosis. There was no lardaceous change. The spleen was enlarged, weighing 16 ounces, and contained a large fibrous area in its centre. The œsophageal veins were dilated. The testes and kidneys were healthy. The liver is in St. George's Hospital Museum, Series ix. 174. I, and was described by Dr. Lazarus-Barlow.*

Diagnosis.—It may be difficult to differentiate between these cases of cirrhosis in individuals with other manifest signs of congenital syphilis, on the one hand, and cases of tardive hereditary syphilis with hepatic lesions and ascites, on the other hand. In the latter there may be excessive lardaceous disease, as shown by albuminuria. Iodide of potassium and mercury should be tried, and improvement will point to hepatic gummata and cicatrices due to tardive hereditary syphilis, and the treatment must then be pushed.

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* Lazarus-Barlow, W. S.: Trans. Path. Soc., vol. l, p. 146.

The **prognosis** of these cases is very bad.

The *treatment* is that of ordinary cirrhosis, viz., milk diet, no alcohol or irritating food. Constipation should be prevented by seeing that plenty of water is taken, and if necessary by calomel and saline purges. Flatulence and excessive intestinal fermentation and putrefaction should be prevented by relieving constipation or by minute doses ($\frac{1}{20}$ to $\frac{1}{40}$ grain) of calomel or of perchloride of mercury. The iodides of potassium, sodium, and ammonium should be given, as is often done in common cirrhosis of adults, to prevent if possible any further progress in the disease. But as the lesion is parasyphilitic rather than syphilitic, iodide of potassium can hardly be expected to remove the fibrosis. In other respects the treatment is on the same lines as in portal cirrhosis.

ACTINOMYCOSIS.

Incidence.—Actinomycosis (ἀκτίς, "a ray," μύκης, "a fungus") is rare in Great Britain and America; less so in Germany, Austria, and Russia. In France its reputed rarity appears to be due to the disease having escaped recognition; Duvau[*] has collected 146 cases observed in that country. In 1902 Erving[†] collected 100 cases in America. In 1094 cases of human actinomycosis collected by Ruhrah,[‡] 604, or 56 per cent., were in the head and neck, 223, or 20 per cent., in the digestive tract, 164, or 15 per cent., in the respiratory tract, 26, or 2 per cent., in the skin; and 63, or 6 per cent., were doubtful.

Actinomycosis is about three times commoner in men than in women.

On the basis of 405 cases Leith[§] estimated that 73 per cent. were males and 27 per cent. females.

It is most frequent between the ages of twenty-five and forty-five years.

The fungus may gain access to the alimentary canal in food; milk from cows whose udders have been infected from contact with straw (Müller[‖]) may spread the disease. The disease is commoner in agriculturists who are more likely to chew ears of wheat, barley, or straw.

Actinomycosis of the liver is rare. It is, indeed, rather surprising that Auvray[**] has only been able to collect records of thirty-one published cases, and he disputes the correctness of Duvau's statement that forty cases have been published.

Method of Origin.—Actinomycosis of the liver must be either metastatic, the infection being conveyed by the blood-stream from a mucous or cutaneous surface, or due to the direct spread of the disease from a focus in the neighbourhood. In the majority of instances the primary focus is in the alimentary canal, from which infection may spread either by the blood-stream or by continuity. In the latter event there may be a mass of inflammatory tissue extending between the affected part of the bowel, usually near the cæcum, and the liver. In rare instances there is a direct spread of the actinomycotic growth from the skin of the abdominal wall or from the base of the right lung into the liver. In some instances the primary focus, usually in the intestine, has healed so that it is very difficult or impossible to determine its situation. It is to such cases, of which Aribaud collected seven, that the term primary actinomycosis of the liver has been applied.

[*] Duvau: Thèse Lyon, No. 92, 1902. La Presse Médicale, May 7, 1902.

[†] Erving, W.: Johns Hopkins Hosp. Bull., Nov., 1902, p. 261.

[‡] Ruhrah: Annals of Surgery, Oct. and Nov., 1899.

[§] Leith: Edinburgh Hospital Reports, vol. ii, p. 121, 1894.

[‖] Müller: Munch. med. Wochen., Dec. 18, 1894.

[**] Auvray: Rev. de Chirurg., tome xxiii, 1903.

In 30 cases of hepatic actinomycosis collected by Aribaud[*] the growth was derived from the intestinal tract in 20. In 12 of these it spread by metastases and in the remaining 8 by direct extension.

As shown by Ruhrah's statistics, more than half the total number of cases of human actinomycosis occur in the head and neck. The liver is very seldom affected in these cases; though it is quite conceivable that when an actinomycotic abscess discharges into the mouth, secondary infection of the gastro-intestinal tract, and so of the liver, might result.

Moodie[†] has recorded a case where a small circumscribed primary actinomycotic tumor of the upper jaw gave rise to a large actinomycoma of the liver.

Actinomycosis or ray fungus belongs to the streptothrix group and presents pleomorphous characters. It may appear as filaments, as cocci, or clubs. The clubs are often absent in human actinomycosis. For a description of the parasite the reader should refer to bacteriological textbooks. Cases of other varieties of streptotrichosis have been described under the name of actinomycosis, and also under the unfortunate title of pseudo-actinomycosis. (Berestnew,[‡] Habershon and Hichens.[§])

MORBID ANATOMY.

The liver is enlarged and shows adhesions on the surface. The morbid condition shows very considerable variation. The actinomycotic abscess has a characteristic honeycombed aspect and has been compared to a sponge soaked in pus. The alveolar appearance is due to the coalescence of a number of small abscesses. The suppurative process spreads by continuity, and is accordingly more or less localised, but sometimes small abscesses are seen away from the main collection, while there may be merely multiple abscesses, like those seen in pyæmia.[‖] The individual abscesses vary in size from a pin's head to that of a walnut.

There is a great tendency to get inflammation of the capsule of the liver and adhesions to adjacent organs. When the actinomycotic lesion is situated anteriorly, it readily extends, after adhesions have been formed, to the abdominal wall and may lead to an abscess. This may be the first evidence of disease, so that caution is necessary in assuming that the hepatic lesion is secondary to an abscess of the abdominal wall. If an actinomycotic abscess near the surface of the liver ruptures into the general cavity of the peritoneum, acute peritonitis will result, as in Grainger Stewart and Muir's[**] case. But from the frequency with which perihepatic adhesions are found it is more usual to get localised collections of pus near the liver, such as a subphrenic abscess. An actinomycotic abscess may even perforate into the stomach.

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[*] Aribaud: Thèse Lyon, 1897.

[†] Moodie, E. L.: Journ. of Path. and Bacteriol., vol. viii, p. 239, 1902.

[‡] Berestnew: Centralblatt f. Bakt., 1899, Bd. xxvi.

[§] Habershon and Hichens: Brit. Med. Journ., 1900, vol. ii, p. 1499.

[‖] Stewart, F. J.: Guy's Hospital Reports, vol. liv, p. 303.

[**] Grainger Stewart and Muir: Edinburgh Hospital Reports, vol. i.

Duckworth and Marsh* met with a case where an actinomycotic abscess in the left lobe of the liver and a subphrenic abscess of the same nature had eroded the stomach wall from without inwards.

The abscess or abscesses in the liver may work their way through the diaphragm into the lung or pleural cavity. Cases of hepatic actinomycosis may thus first present themselves as chronic empyemata of obscure origin. When the actinomycotic tumor is in the posterior part of the right lobe, it may spread into the right suprarenal body, and even reach the right kidney.

The pus contains the characteristic granules composed of the ray fungus—actinomycotic colonies—and numerous pyogenetic cocci. Stewart considers that suppuration is due to secondary infection and that it does not occur until this has taken place. Suppuration may, however, be found to be associated with apparently pure streptothricial infections.

Around the areas of suppuration there is fibrosis with pigmentation of the walls of the abscesses. Microscopically there are intercellular fibrosis and atrophy of the liver cells. The remainder of the liver may be fatty or lardaceous. In rare cases actinomycosis may be pyæmic and spread by the blood-vessels.

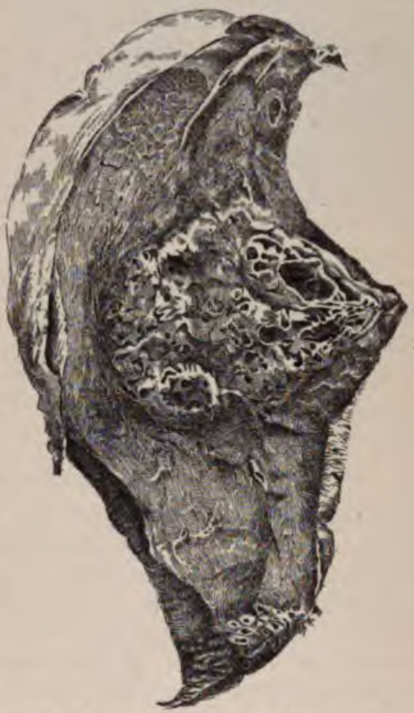

FIG. 48.—ACTINOMYCOSIS OF THE LIVER, FROM A SPECIMEN IN ST. GEORGE'S HOSPITAL MUSEUM. (Drawn by Dr. E. A. Wilson.)

In Kanthack's † case it was not clear whether the abscess originated in the right lobe of the liver or at the base of the right lung; from this it had spread by continuity into the right suprarenal body, and had given rise to secondary pyæmic abscesses over the body. In Boari's ‡ case there were secondary pyæmic abscesses due to pyogenetic cocci and not containing actinomyces.

Actinomycotic lesions in the liver have sometimes been regarded as tuberculous or ordinary hepatic abscesses.§

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* Duckworth and Marsh: Brit. Med. Journ., 1900, vol. ii, p. 1189.

† Kanthack: Trans. Path. Soc., vol. xlv, p. 233.

‡ Boari: Il Policlinico, 1897, p. 19.

§ *Vide* Harley, Medico-chirurg. Trans., vol. lxix, p. 135. Shattock: Trans. Path. Soc., vol. xxxvi, p. 260.

CLINICAL PICTURE.

Before there are any symptoms or signs indicating disease of the liver there may be evidence of abdominal disturbance, such as pain, constipation, or localised swelling imitating appendicitis. Stewart has laid stress on the occurrence of two stages in the disease—an early period just referred to, and a later one when the liver is definitely affected. Between these two stages there may be an interval of fair health. The first symptoms of hepatic actinomycosis may be those of an empyema, of an abscess in the abdominal wall, or, when the portion of the liver near the kidney is involved, of a perinephritic abscess. The liver may be enlarged, and with a slight degree of fever and pain over the liver the resemblance to an ordinary hepatic abscess may be very close. Jaundice is extremely rare.

Ascites has been noticed to occur late in the disease (Eve*), but is usually absent. Anæmia of a chlorotic type, viz., diminution of the red blood-corpuscles with a greater reduction in the amount of hæmoglobin, is an important feature of the disease. There is leucocytosis.

Latimer and Welch † described a case of actinomycosis of the liver combined with myelogenous leukæmia.

PROGNOSIS.

The prognosis of actinomycosis of the liver is very bad. Duvau,‡ a pupil of Poncet, collected 40 cases of hepatic actinomycosis, all of which proved fatal. Presumably the prognosis should be less gloomy if the disease could be recognised in an early stage and treated vigourously with iodide of potassium, and secondary infection with pyogenetic cocci prevented. For when the latter event has occurred the prognosis is bad. Though much commoner in animals, actinomycosis is rather more virulent in man.

DIAGNOSIS.

The diagnosis depends on finding the fungus in the pus either from the liver or from a discharging abscess elsewhere. Before this has been done the condition is hardly likely to be thought of, and recorded cases show that the disease has been regarded as empyema, phthisis, sarcoma of the kidney (Leith), perinephritic abscess, hepatic abscess, suppurating hydatid, or gumma of the liver. It has been observed that the subjects of actinomycosis react to Koch's tuberculin (Kahler, Arloing); this might lead to an erroneous diagnosis of that very rare condition, massive tubercle of the liver.

TREATMENT.

The effect of iodide of potassium, introduced by Thomassen, on actinomycosis is extremely marked and does fully as much good as it does in tertiary syphilis. It should be given in large doses, as much as two drachms or even more daily. Sawyer * has urged that, in addition to its administration by the mouth, iodide of potassium should be injected directly into the affected part; 15 to 30 minims of a 1 per cent. aqueous solution of iodide of potassium are injected into the area infected with actinomycosis; at first this is done at intervals of three or four days, but after a time the injections can be given more frequently.

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* Eve: Trans. Path. Soc., vol. xl, p. 405.

† Latimer and Welch: Trans. Assoc. Americ. Phys., vol. xi, p. 328.

‡ Duvau: Thèse Lyon, 1902. Abstract La Presse Médicale, May 7, 1902.

When an actinomycotic abscess has been opened, the necrotic tissue may be scraped away with advantage, while of course iodides should be given freely. Iodoform may be employed locally, and carbolic acid or other disinfectants should be applied in order to minimise the risks of septic infection. In a few cases tuberculin has seemed to have a good effect, while Ziegler has found the injection of a proteid body obtained from cultures of Staphylococcus pyogenes aureus of use. Arsenic has also been recommended (Braun).

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* Sawyer: Journ. American Med. Assoc., May 11 1901

LYMPHADENOMA AFFECTING THE LIVER.

Synonym: Hodgkin's Disease.

In generalised lymphadenoma the liver may contain nodules of white growth. As a rule, the growths are small, discrete, and do not lead to any enlargement of the organ during life. In exceptional cases, as in a boy aged six years under the care of my colleague, Dr. Penrose, with generalised lymphadenoma, there may be a large diffuse mass of growth in the liver.

In a new-born infant the pleuræ, peritoneum, intestines, bladder, and suprarenal bodies contained growths regarded by Bouvain and Ducloux* as lymphadenoma. The liver was greatly enlarged from numerous nodules of growth. Such a case closely resembles generalised sarcoma.

Morbid Anatomy.—The appearances of lymphadenomatous nodules in the liver may imitate caseous tuberculous masses and secondary new-growth. They are firm, white, and do not show any softening or bile-staining; in these particulars they differ from what is often seen in advanced caseous tubercles. Tuberculosis may, however, be implanted on lymphadenoma.

In a boy aged sixteen years, who had extensive lymphadenomatous lesions, the liver, which was lardaceous without any definite cause, such as syphilis or suppuration, contained small caseous tubercles in which tubercle bacilli were demonstrated (Dickinson †).

The combined lesions of lymphadenoma and tuberculosis may be found in the liver (Andrewes ‡), as is well shown in a specimen (No. 2223^{c}) in St. Bartholomew's Hospital Museum. Lardaceous change may be found in a liver affected with lymphadenoma, and from the absence of any recognised cause, such as suppuration or syphilis, it would appear that lymphadenoma, or its underlying cause, may induce the lardaceous change.

Microscopical Appearances.—The growth starts in the portal spaces and extends outwards, passing between and eventually into the neighbouring lobules. The margin of the invaded lobules has an appearance like that of intercellular cirrhosis. Gradually the growth replaces the lobules, as the result of atrophy of the liver cells which may be seen for a time embedded in the growth. The columns of deeply staining cubical cells, the so-called new bile-ducts, show up prominently both in the growth and at its advancing margin. They are the result of an attempt at compensatory hyperplasia of the liver cells. In an early stage the growth is composed of proliferated endothelial cells which may show several nuclei—lymphadenoma cells, leucocytes, and young connective-tissue cells. A little later there is a distinct reticulum to be made out,

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* Bouvain and Ducloux: La Presse Médicale, July 13, 1901.

† Dickinson, W. L.: Trans. Path. Soc., vol. liii, p. 315.

‡ Andrewes, F. W.: Trans. Path. Soc., vol. liii, p. 313.

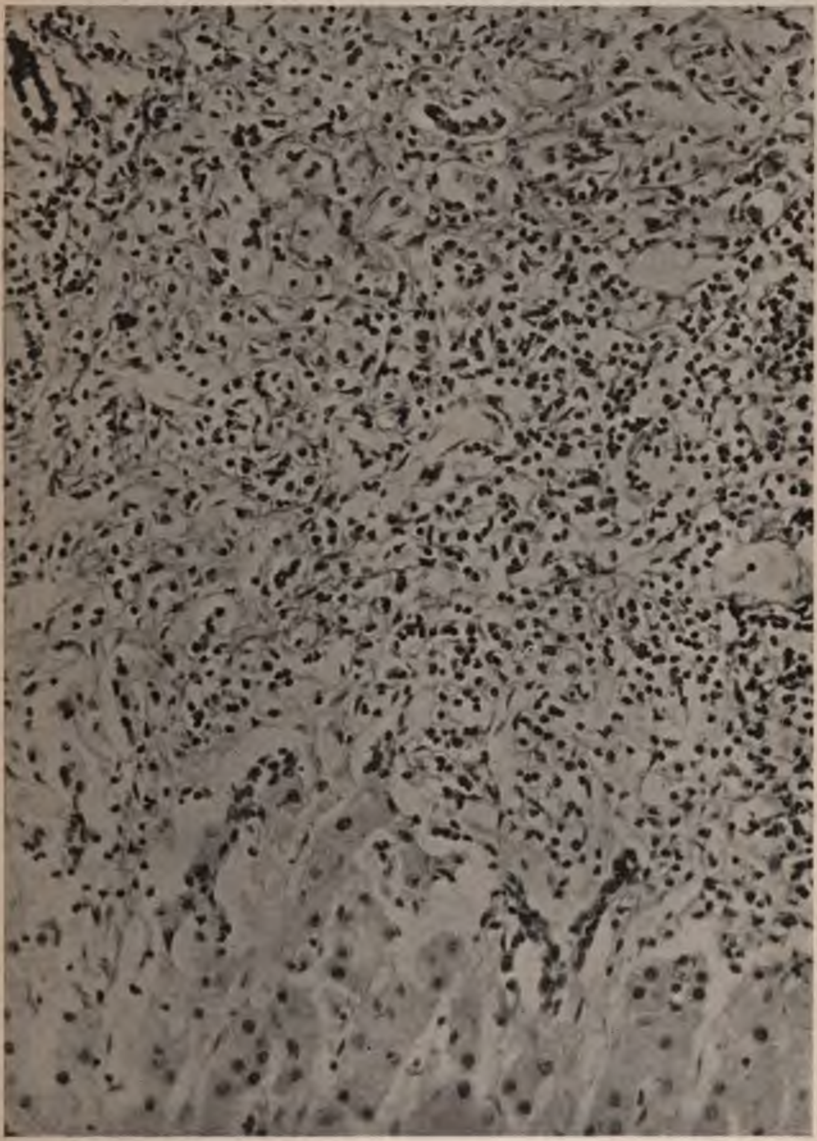

FIG. 49.—MARGIN OF LYMPHADENOMATOUS NODULE.

The endothelial and connective-tissue cells forming the growth are well seen. There is a reticulum between the cells. In one part the formation of deeply staining pseudobile canaliculi from the liver cells can be seen. High power. (Dr. H. Spitta.)

and as time goes on the network increases in amount and the growth becomes more and more fibrous. For a full description of the histology of lymphadenoma the reader should consult Andrewes', Reed's,[*] and Longcope's[†] papers.[‡]

There is seldom any **clinical evidence** that lymphadenoma has involved the liver, apart from slight enlargement, and this is not common. Exceptionally the organ is very considerably enlarged, and if the superficial lymphatic glands available for clinical examination are but little affected, the clinical aspect of the case, especially when there is a hectic temperature, may suggest hepatic abscess, as in a case under my care. Suchard and Teissier[§] met with a case suggesting carcinoma of the liver.

Ascites may be present, but may be due to involvement of the intra-abdominal lymphatic glands and lymphatic obstruction; in such cases the effusion may be milky and resemble chyle. Jaundice does not often occur, although enlarged glands in the portal fissure may be so close to the bile-duct as to render it probable.

The **treatment** is the same as in lymphadenoma, but the **prognosis** is very bad when the liver is involved.

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[*] Johns Hopkins Hosp. Reps., vol. x, p. 133.
[†] Bull. Ayer Clin. Lab., No. 1, 1903.
[‡] Trans. Path. Soc., vol. liii, p. 305.
[§] Suchard and Teissier: Bull. Soc. Anat. Paris, 1897, p. 940.

HYDATID CYSTS.

Hydatids (ὑδατις) of the liver are the cystic, larval, or bladder stage of a tapeworm which in its adult stage is found in the intestine of the dog; they also occur in the wolf, the fox, and the jackal.

Life-history.—This tapeworm—the tænia echinococcus—is small, measuring about 4 millimetres, or ⅙ inch, in length, and composed of not more than four segments or proglottides, the last or terminal one being larger than the others put together, and containing fully developed sexual organs and, when fecundated, ova to the number of 500. The first segment, or head, has a prominent rostellum surrounded by two rows of hooklets, there being about 20 hooklets in each series. There are also four suckers. When the terminal proglottis breaks off from the tapeworm and is carried along with the fæces, the contained ova become liberated.

The ova after their exit from the bowel of the host become scattered about, and may find their way into the alimentary canal of man, from being eaten on lettuce, water-cress, or other vegetables, or drunk with water. When the ova get into the stomach, their chitinous envelopes are dissolved, and an oval-shaped embryo, with six spines arising from one of its poles, is set free. The spines are directed backwards and thus allow the embryo to bore its way into the coats of the bowel, but prevent it from returning back along the passage it has made. The embryos get into the portal vein and are conveyed to the liver. That they pass by the portal vein is largely assumed because the liver is *par excellence* their destination. If they simply bored their way straight through opposing structures, it would be natural to find them equally distributed throughout the surrounding organs. Possibly, moreover, conditions for their further development are more favourable in the liver than elsewhere, just as in the case of the free embryos of trichina the muscles are the place of selection.

It has been thought, and very probably with truth, that any blow or traumatism of the liver will favour the evolution of an embryo into a hydatid cyst by reducing the resistance of the liver and so allowing the parasite every chance of development. The passage of the embryo through the walls of the stomach is not attended by any recognised symptoms.

When the embryo reaches the liver and comes to rest, it proceeds to become transformed into the bladder or hydatid. The embryo loses its hooklets and enlarges so as eventually to form a small cyst; the outer surface becomes laminated and is called the ectocyst, while more internally the granular endocyst is evolved, and the contents undergo liquefaction. When reproductive changes leading to the production of daughter cysts commence, the first change is the formation of brood-capsules in the endocyst. These are small buds, lined internally by material resembling the ectocyst, and externally by the endocyst, so that it appears like an invagination of the cyst. The cavity of the brood-capsule contains fluid. From the outer surface of the brood-capsule the scolices develop; they are the early stage of the head of the future tapeworm and are provided with hooklets. The scolices arising from the outer surface of the brood-capsule eventually become invaginated into its interior. They readily become detached from the wall of the brood-capsule, and as a result of rupture of the brood-capsules become free in the cavity of the cyst. A scolex is about 0.3 mm. long and consists of two segments; the segment originally attached to the wall of the brood-capsule often contains crystals of carbonate of lime, while the free segment has a crown of hooklets and four suckers. The hooklets measure 0.04 mm. Should the scolex reach the intestine of a dog it develops into an adult tapeworm by lengthening and transverse segmentation of its posterior end.

Daughter cysts are produced either inside the original cyst, endogenous formation, which is the usual way, or more rarely by external budding off, exogenous formation. The daughter cysts are derived from either the scolices or brood-capsules, which become vesicular, or from invagination of the parenchymatous endocyst. The daughter cysts may become detached from the endocyst and become free in the cavity of the parent cyst, and may contain granddaughter cysts.

Exogenous formation of daughter cysts is rare in man, though common in sheep. Cysts are formed in the deeper layers of the ectocyst, become filled with fluid, and work their way outwards; they finally project from the surface of the mother cyst and become surrounded by a fibrous adventitious capsule. The mother cyst thus becomes knobby from the projection of daughter cysts, some of which may become disconnected from it. It is possible, however, that the so-called exogenous appearance is really only due to the cyst growing irregularly and sending out processes in the lines of least resistance. Pseudopodial-like processes of a single cyst might thus travel along the portal spaces in the liver, there being a continuous cavity throughout. Later the communication between the cyst and its process might become constricted, and in this way the appearance of a secondary cyst attached to the main cyst, but with an independent cavity, might be produced.

It has been thought that the extremely rare disease, multilocular hydatid, is a form of the exogenous proliferation of the hydatid cyst. In connexion with the exogenous mode of growth it may be pointed out that the presence of two or more hydatid cysts in the same liver is probably due to two distinct embryos having reached the liver and not to exogenous formation of one from the other.

Sterile Hydatid Cysts.—If no multiplication or reproductive changes take place in the cyst, it is spoken of as being sterile or as an acephalocyst, though the latter term is not often used now. The fluid contains no daughter cysts or scolices, and the nature of the cyst, whether hydatid or not, must be determined by microscopic examination of its wall. Failure in reproduction probably depends on imperfect nutrition. Pedunculated hydatid cysts that hang down from the under surface of the liver are more likely to be sterile than those embedded in the substance of the liver.

Warty ingrowths from the cyst wall are sometimes observed; they are probably abortive daughter cysts.

In the museum of Surgeons' Hall, Edinburgh, there is a part of the wall of a hydatid cyst showing extremely well this papillomatous appearance. The cyst was a large one and contained many hundreds of small cysts. (No. 1885.)

On the other hand, it is possible that in some of the cases the warty growths were due to commencing degenerative changes and that the process is due to involution and not to imperfect evolution.

STRUCTURE OF HYDATID CYSTS.

The wall of the true parasitic cyst consists of the outer cuticle, or ectocyst, and an inner lining, or endocyst. The cysts have an opalescent whitish-blue colour, and unless considerably thickened, tear easily. The ectocyst is elastic and tends to curl up when it is incised. Structurally it has a very characteristic laminated appearance. There are wavy bands of homogeneous, hyaline material which, like the wall of the original ovum, is chitinous.

The endocyst forms the parenchymatous or granular internal lining of the ectocyst; from it the brood capsules are developed. It may contain crystals of carbonate of calcium like those seen in the mature cestoda and in the scolices. The fluid in a living hydatid cyst is clear, of a low specific gravity, 1002 to 1010, contains no albumin, but a considerable quantity of chloride of soda; for other details see page 402 (diagnosis by examination of fluid). When the cyst becomes inflamed or dies, it contains albumin and may be turbid.

Outside the parasitic cyst, as a result of compression and irritation of the tissues of the liver, a fibrous capsule is produced which extends for a short distance into the surrounding liver substance. When a hydatid cyst projects from the surface of the liver, a thick fibrous covering of the consistence of cartilage may develop over the cyst, which resembles a corneal fibroma of the spleen, and may show calcification. The remains of the hydatid cyst may escape notice, and the true nature of these thick-walled cysts be overlooked. When embedded in the substance of the liver the fibrous capsule shows columns of small cubical cells, pseudo-bile canaliculi, due to hyperplasia of included liver cells. In addition, there may be giant cells whose function is to attempt absorption of the cyst; they do not contain tubercle bacilli and differ from the giant cells of tuberculous granulation tissue in that their nuclei are in the centre and not at the periphery.

When two cysts arise in close contact to each other, they may be enclosed in the same pseudocyst or capsule derived from the tissues of the liver by pressure irritation. Occasionally an hydatid cyst is found to be divided into two parts by a constriction, and thus to resemble an hour-glass or a shirt stud. This may depend either on two cysts, originally separate, opening into each other, or, as pointed out in speaking of exogenous formation of daughter cysts, on irregular growth due to differences in the resistance offered by the surrounding tissues.

Grange * describes a suppurating hydatid cyst in the liver shaped like a shirt stud, with a small superficial cavity communicating by a constriction with a larger and more deeply seated cavity.

Situation of Hydatid Cysts in the Liver.—The cysts may be deeply and entirely embedded in the liver, and are naturally, from the greater size of the right lobe, commoner there than in the left lobe. Cysts arising from the upper and back part of the right lobe push the diaphragm up and may imitate a pleural effusion. When the cyst is deeply placed and expands and pushes the liver forwards, the condition in some ways resembles a solid growth of the liver. Not uncommonly a hydatid cyst hangs down from the under or lower surface of the liver and may resemble a dilated gall-bladder.

Number of Cysts.—There may be only one cyst in the liver, but it is not by any means rare to find two or three. Large numbers of small cysts have been found in the liver; forty (Dolbeau †) or even a hundred have been seen in the same liver (Murchison ‡).

Size.—A single hydatid cyst may reach a very large size indeed. The largest hydatid cyst of the liver on record appears to be one containing 36 pints; it occupied three-quarters of the abdomen and was successfully operated upon by H. B. Robinson; § four years previously it had been tapped and 40 litres (70 pints) removed with only very temporary relief.

Spontaneous Death.—Inasmuch as hydatids are most commonly present in the liver, being found there in 57 per cent. of all the cases of the disease, it is natural that hydatid cysts which have become latent and undergone involution changes ending in spontaneous cure are commoner in the liver than elsewhere.

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* Grange: Lyon Médical, tome xcii, p. 22, Sept. 3, 1899.
† Dolbeau: Bull. Soc. Anat. Paris, 1857, p. 116.
‡ Murchison, C.: Diseases of the Liver.
§ Robinson, H. B.: Trans. Clinical Soc., vol. xxx, p. 16.

It has also been thought that they are more often found in the liver because their natural evacuation is less easy than in the case of the lung or kidney, from which they may be coughed up or passed into the ureter. But with regard to this it may be said that there is not much difference between the lumen of the common bile-duct and of the ureter, except that the larger end of the ureter, the pelvis of the kidney, is directed towards the hydatid in the kidney, while the intra-hepatic bile-ducts are small. But this explanation of the frequency of hepatic hydatids is not worth much, for natural evacuation is rare in any organ and much less common in the lung and kidney than in the liver.

Causes of Spontaneous Death.—Possibly the cause may sometimes be inherent in the individual parasite, which, being of poor vitality, runs its allotted course and dies before having reached the ordinary size. For death with spontaneous cure is most often seen in small cysts which have not given rise to symptoms during life. This, however, is not a universal rule, and a large hydatid, if not operated on, may gradually undergo involution changes and shrivel up.

A remarkable example is recorded by Murchison.* A patient had been seen when eleven years old by Sir Ashley Cooper, and his liver was then said to be four times its natural size and was thought to contain fluid; there was some question of an operation, but this was not done. The tumor gradually got smaller and forty-five years later, when Murchison saw the case, there was a mass as hard as bone in connexion with the right lobe of the liver.

The usual term of life of a hydatid cyst is not known, but it has been thought to be as long as twenty years. Of the causes acting from without and impeding the growth or possibly poisoning the parasite outright, the most commonly recognised is the entrance of bile into the cyst. The constant pressure exerted by the contents of the tense cyst leads to atrophy of the tissues intervening between the cavity of the cyst and an adjacent bile-duct and allows of the entry of bile into the cyst, and sometimes of a discharge of the contents of the cyst into the bile-duct. (*Vide* Rupture of Hydatid Cysts into Bile-ducts.) As evidence of the entrance of bile into the cyst the occurrence of crystals of bilirubin and biliverdin may be forthcoming.

On the other hand, dead cysts may not contain any trace of bile, while spontaneous cure of hydatid cysts may occur in other organs, where, of course, bile can play no part. Further, it would appear that the parasiticidal action of bile is slight, as Dévé † finds that scolices continue to grow in a mixture of hydatid fluid and bile even when equal quantities of bile and hydatid fluid are used. Secondary hydatid cysts can develop in the peritoneum when there is a bile-stained peritoneal effusion from rupture of a hydatid cyst, already communicating with a bile-duct, into the peritoneal cavity. It therefore seems probable that bile has little to do with spontaneous death of hydatid cysts in the liver. In some instances the entrance of bile is subsequent to the death of the parasite.

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* Murchison: Lectures on Diseases of the Liver, p. 130, 1877.

† Dévé: Soc. de biolog., Jan. 17, 1903.

Chemical alterations in the lymph bathing the outside of the cyst have also been suggested, and it has been thought that poisonous products absorbed from the bowel, such as alcohol, might play some such part; but the resistance of hydatid cysts to any form of drug renders this doubtful. The entrance of fluids, such as blood, into the cavity of the cyst may so disturb the equilibrium necessary for the continued life of the parasite as to lead to its death. Of the occurrence of past hæmorrhage into a hydatid cyst there is no very satisfactory evidence, as the crystals of hæmatoidin and bilirubin are identical. It appears probable that in cases where "hæmatoidin" is described as being found in cysts the crystals are really bilirubin.* Absorption of the contained hydatid fluid has been thought to be the cause of spontaneous death of the parasite; this view is supported by cure after simple tapping of a cyst, but, on the other hand, there is no proof that under ordinary conditions absorption of the fluid can occur from a living cyst.

The rapid proliferation of the daughter cysts so that they increase out of all proportion to the surrounding fluid and produce heightened pressure, and so exert an inhibitory influence on the life of the parasite, has been put forward as a cause of spontaneous death.† That this is not a universal cause is shown by the fact that dead cysts may contain few or even no daughter cysts. Changes in connexion with the fibrous capsule of the cyst, such as cicatricial contraction and calcification, have also been thought to interfere with the nutrition of the parasite, but it is difficult to prove the relationship between the two processes.

Changes Following the Death of a Hydatid Cyst.—The fluid of a living hydatid cyst under ordinary conditions is practically free from albumin; after death, however, it becomes albuminous. From the albuminous fluid removed from a hydatid cyst which had previously been killed by electrolysis Boinet‡ obtained crystals of a toxic body analogous to myrtilotoxin, probably the result of cleavage of the albumin. The albuminous fluid in the cyst becomes turbid and cloudy from the precipitation; as time goes on absorption occurs and the contents get less fluid and more gelatinous and the parent cyst shrinks, while fatty metamorphosis of the albumin gives the contents a buttery, caseous, or putty-like character; various stages, from a glairy or colloid state to complete solidity, may be met with as time goes on. The contents are frequently yellow in colour. These changes in the mother cyst are later on repeated in the daughter cysts. The putty or gelatiniform material may contain crystals of cholesterin, stearin, bile pigment, tyrosin,§ and calcification may extend from the outer adventitious capsule into the contents of the cyst.

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* *Vide* Dickinson, W. L.: Trans. Path. Soc., vol. xlv, p. 259.

† Murchison: On Diseases of the Liver, 1885, p. 62.

‡ Boinet: Rev. de Méd., 1898, p. 845.

§ Carwardine: Path. Trans., vol. xlix, p. 132.

Contraction and shrinking of the outer fibrous capsule lead to a folding of the cyst wall compared to the appearance of a corpus luteum. The outer capsule may become extremely hard from infiltration with carbonate and phosphate of lime. Good specimens of the calcified shells, so to speak, of hydatid cysts are to be found in most museums; there is one (No. 2234) in St. Bartholomew's Hospital Museum of multiple calcified cysts. Usually the process of spontaneous cure is unaccompanied by any inconvenience or clinical signs.

In a case recorded by Mitchell Bruce and Sheild* a very large cyst underwent changes resulting in a gelatiniform condition of its contents. The tumor was so large, and was, contrary to what would naturally be expected, increasing in size, that laparotomy was performed. The diagnosis of a solid hydatid cyst had previously been made certain by aspiration of some of the colloid matter containing hooklets.

In rare cases a spontaneously cured hydatid may undergo suppuration and, if it communicates with the bile-ducts, be the cause of suppurative cholangitis.

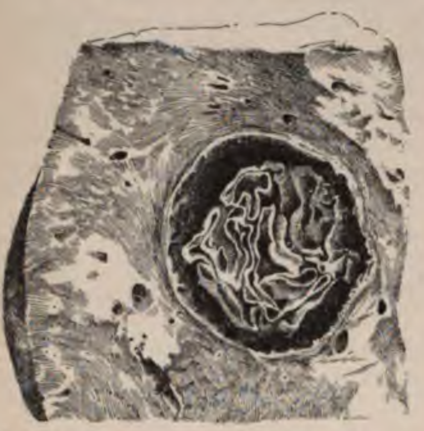

FIG. 50.—DRAWING OF AN OBSOLETE HYDATID CYST IN THE LIVER.

From a specimen (series ix, No. 179e) in the Museum of St. George's Hospital. (Drawn by Dr. E. A. Wilson.)

Condition of the Remainder of the Liver.—The pressure exerted by a large cyst causes atrophy of the part of the liver in its immediate neighbourhood, and in this way a whole lobe may become excavated and destroyed. In extreme instances the organ may become so deformed that its anatomical features are quite obliterated. Compensatory hypertrophy of other parts of the liver readily occurs, and the resulting hypertrophy is often considerably in excess of the normal amount of liver substance. The left lobe has been found to weigh as much as a normal liver. (Chauffard.†) The compensatory hyperplasia occurs with greater ease in hydatid disease of the liver than in cirrhosis, malignant disease, or abscess. This is probably because there is no depressing factor, such as the presence of toxines, to reduce the vitality and health of the liver cells. The compensatory hypertrophy is better developed at some distance from the cysts, and since cysts are usually in the right lobe, the left is frequently greatly hypertrophied, though the quadrate and spigelian lobes share in the compensatory process. This compensation accounts for the marked absence of constitutional symptoms in the disease. With very rapidly growing hydatid cysts there may not be time for compensatory hypertrophy to occur, and the amount of liver substance may for a time be greatly diminished. As a coincidence, hydatid cysts have been found to be associated with universal cirrhosis of the liver (Cayley, Weir, S. Savage [*]), and with malignant disease.[†] In a man at forty-nine who died in St. George's Hospital from pyloric carcinoma with extensive secondary infection of the liver, which weighed 10 pounds, there was a dried-up hydatid cyst in the right lobe close to the gall-bladder. In a case recorded in St. Thomas' Hospital Reports primary carcinoma of the liver was associated with several calcified hydatid cysts.[‡] But there is no reason to think that these conditions are secondary to the irritation exerted by the cyst.

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* Mitchell Bruce and Sheild: Medico-Chirurg. Trans., vol. lxxv, p. 175.

† Chauffard: Archiv. Gén. de Méd., 1890.

In a case recorded by Pitt[§] the irritation set up by a cyst in the left lobe of the liver of a man aged thirty-nine years, who had contracted syphilis thirteen years before death, seemed to have given rise to a remarkable syphilitic growth enclosing the cyst.

Relative Frequency of Hepatic to Hydatid Cysts Elsewhere.—The liver is more often the site of hydatid cysts than the whole of the remainder of the body. The percentage incidence of hydatids in the liver is variously estimated at 74 per cent. (Lyon[‖]) to 44 per cent. (Davaine.[**])

In 1897 cases of hydatid disease Davies Thomas[††] found the liver affected in 1084, or 57 per cent., the lungs being next with 220, or 11.6 per cent. Finsen estimated the incidence of hydatids in the liver at 69 per cent., Peiper[‡‡] at 66.4 per cent., Neisser[§§] at 50 per cent., and Cobbold, on the basis of his own and Davaine's cases, at 46 per cent.

The great frequency with which the liver is affected is due to its filtering the blood from the intestines and thus arresting the embryos which have got into the portal vein. If the embryo is not stopped by the liver, it passes to the capillaries of the lung and may come to rest there.

ETIOLOGY.

Geographical Distribution.—In England hydatid disease is said to be commoner in London than in most country districts, but in the Fen districts around Cambridge hydatids are comparatively common.

Murchison in 2100 postmortem examinations at the Middlesex Hospital records 13 bodies in which hydatids were found, or 1 in 161; in 7 of these, or 1 in 300, they were the cause of death. From an examination of the statistics of in-patients at St. Bartholomew's Hospital for thirty years Sir. W. Church[‖‖] found that one case of hydatid disease was admitted in 1100.

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[*] Cayley, W.: Trans. Path. Soc., vol. xxv, p. 129. Savage, S.: Brit. Med. Journ., 1899, vol. i, p. 1030. Weir: Medical Record, Feb. 4, 1899, p. 149. Stevens: Brit. Med. Jour., 1901, vol. i, p. 1139.

[†] Habran: Bull. Soc. Anat. Paris, 1868, p. 437. Florand: Ibid., 1886, p. 677.

[‡] St. Thomas' Hospital Reports, vol. xxix, p. 141.

[§] Pitt, G. N.: Trans. Path. Soc., vol. xxxvii, p. 276.

[‖] Lyon: American Journ. Med. Sciences, vol. cxxiii, p. 124.

[**] Davaine: Traité des Entozoaires, Paris, 1878.

[††] Thomas, Davies: Hydatid Disease, 1894.

[‡‡] Thierische Parasiten, S. 158, 1904.

[§§] Neisser: Echinococcenkrankheiten, Berlin, 1877.

[‖‖] Church, W. S.: Clinical Journal, March 21, 1900.

In Scotland hydatids are very rare, but in Shetland they are comparatively common. (H. Stiles.*) In Russia they are rare. In Switzerland and South Germany they are fairly frequently met with. In Iceland they are extremely common; estimates vary from one-sixth to one-fifty-eighth of the entire population, one-thirtieth being the mean and more probable figure. The great frequency of hydatid disease depends on the enormous number of dogs and on the fact that they are very frequently infected with tænia. Hydatid cysts are rare in Africa, but are becoming more frequent in Algiers. In Australia they are very frequent, being commonest in South Australia. In 1000 postmortem examinations mentioned by Stirling and Verco hydatids were found in 49, or 5 per cent. In Victoria one case of hydatid occurs in every 175 admitted to hospital, in New South Wales 1 in 380, while the proportion in New Zealand and Tasmania is also very high. (Church.)

In North America hydatid disease is rare, and when it is met with is in the bodies of foreigners.

Up to July, 1891, Osler† could only find evidence of 85 cases; since the migration of Icelanders into Winnipeg the disease has become more frequent in that locality. Ten years later Lyon‡ collected notes of 241 cases of hydatid disease occurring in the United States and Canada up to July 1, 1901. Most of the cases were either in Icelanders or in Germans.

In the Argentine Republic hydatid disease has been becoming increasingly common of late years.§ This depends on the large number of cattle and dogs there. Hydatid disease is very rare in India, and doubt has been expressed as to its origin there at all;‖ it may be found in persons dying in India who have acquired the disease elsewhere. W. J. Buchanan ** records an undoubted case of hydatid cyst of the liver in a native of India who had never been out of the country.

There is nothing to suggest that the natives of Iceland or Australia, where the disease is most prevalent, are in the slightest degree immune from hydatid disease. Verco and Stirling †† state that except for accident and tuberculosis, hydatid disease was responsible for all deaths of the aborigines in the Adelaide Hospital.

Method of Infection.—The ova derived from the dried and scattered fæces of dogs may settle on vegetables or contaminate drinking-water. Lettuce and especially watercress may, if not carefully washed, serve as vehicles for the transmission of the disease. Persons in contact with dogs and other animals, the subjects of tænia echinococcus, are in danger of becoming the hosts of the bladder stage of the tapeworm. There is some risk in the possession of pet dogs, as infection may be conveyed by a dog licking the hands and face of its master.

It has been suggested as possible that when portions of hydatid cysts embedded in the livers of sheep or oxen are eaten, the scolices may develop in the alimentary canal of man and give rise to autoinfection. This theory requires for its confirmation the recognition of scolices in the human alimentary canal, and has not yet been justified. Offal from slaughter-houses, however, containing hydatid cysts is a most important factor in the causation of the tapeworm in dogs, and so indirectly of the cysts in man.

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* Stiles, H.: Scottish Med. and Surg. Journ., Feb., 1903.

† Osler, W.: Practice of Medicine, ed. ii.

‡ Lyon: American Jour. Med. Sciences, vol. cxxiii, p. 124.

§ Vegas and Cramwell: Rev. de Chirurg., April, 1901.

‖ Chevers: Diseases of India, p. 624.

** Buchanan: Lancet, 1900, vol. ii, p. 19.

†† Verco and Stirling: Allbutt's System, vol. ii, p. 1114.

Sex.—The incidence of hydatid disease in the two sexes depends on their relative exposure to infection, which is generally more marked for men. In Australia, where, according to Stirling and Verco, the water-supply in the bush is the great source of infection, the ratio is as 100 in men to 77 in women. In America Lyon[*] found the percentage incidence 60 per cent. in man and 40 per cent. in woman. In France Davaine[†] found the incidence equal in the two sexes. In Berlin, however, women were more often affected than man in the ratio of 65 to 35 (Neisser[‡]), and in Iceland women are twice as often affected (71 per cent.) as man (29 per cent.) (Finsen[§]).

Age.—The disease becomes more frequent up to about fifty years of age and then declines. The majority of cases occur between twenty and forty years of age. It is rare under fifteen years of age, and it is probable that only 5 per cent. of the total number of cases occur under ten years of age. When children are affected, it is said to be less rare in girls than in boys, and to attract attention chiefly about eight years of age.

Pontou[‖] collected 22 cases in children in 1867, and a large number have since been recorded. In eight years Broca[**] operated upon nine cases. Cases of two cysts in the liver of a boy aged six years (H. B. Robinson[††]) and a boy aged seven years (Cheney[‡‡]) have been recorded. In Cheney's case one of the cysts was suppurating.

CLINICAL PICTURE.

Symptoms.—A hydatid cyst of the liver may remain entirely latent, so that its presence, even when the changes of involution or spontaneous cure have not supervened, may be only revealed at the autopsy, or be suspected for the first time when the abdomen is examined, in the course of life insurance routine or in a pregnant or recently delivered woman. Even when the cyst is large, there may be nothing to attract the patient's attention, except perhaps the increasing size of the abdomen. In some instances there may be a feeling of weight or of dragging in the region of the liver. When the peritoneal covering of the liver is inflamed, tenderness and pain on respiration are present, but acute perihepatitis is infrequent in hydatid disease in the absence of suppuration. The contrast between the marked physical signs and the freedom from symptoms and from constitutional disturbance has already been referred to. Pressure symptoms are, as a rule, absent; this probably depends on the slow growth of the cyst.

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[*] Lyon: American Jour. Med. Sciences, vol. cxxiii, p. 124.

[†] Davaine: Traité de Entozoaires, Paris, 1877.

[‡] Neisser: Die Echinococcenkrankheiten, 1877.

[§] Finsen: Quoted by Lyon.

[‖] Pontou: Thèse Paris, 1867. Quoted in Traité des Maladies de l'enfance. vol. iii, p. 195.

[**] Broca: Sem. Méd., 1901, p. 89,

[††] Robinson, H. B.: Lancet, 1899, vol. i, p. 767.

[‡‡] Cheney: Archives of Pediatrics, Nov. 1897, p. 851.

Pressure on the stomach and intestines, however, may so embarrass these organs as to give rise to dyspepsia, vomiting, and constipation. Obstruction is a most exceptional result of hydatid cysts, but Reichold * has recorded the case of a woman in whom intussusception had been diagnosed. Upward pressure on the diaphragm may greatly encroach on the pleural cavity and produce considerable dyspnœa. This will be more marked when the abdomen is distended from some additional cause, such as pregnancy. The irritation of a large hydatid cyst may set up slight pleurisy and give rise to pain and cough. As in some other hepatic conditions, the pain may be referred to the right shoulder. Epistaxis, hæmatemesis, melæna, and metrorrhagia have been put on record, but are extremely rare.

In a case recorded by Hillier† hæmorrhage took place into a hydatid cyst and ran along the hepatic duct, which also opened into the cyst, to the duodenum. The patient died from the effects of hæmatemesis and melæna. At the autopsy the cyst contained 37 ounces of blood-clot.

The physical signs of hydatid cysts are, unlike what occurs in many diseases, more prominent than the symptoms. In many instances the upper segment of the abdomen on the right side and in the epigastrium is prominent and firm, and there is bulging of the costal arch on the right side. In great abdominal distension lineæ albicantes may be present. Dilated subcutaneous veins are very exceptional, but a prominent "caput medusæ" has been noted when the inferior vena cava is compressed by a large cyst.

The liver is enlarged, its form and outline varying, of course, with the position of the cyst or cysts. When the cyst is near the convexity of the liver, it tends to displace the diaphragm upwards. A cyst in the right lobe may compress the lower lobe of the right lung and imitate a pleural effusion. In rare instances a cyst in the left lobe may simulate a pericardial effusion.

When the cyst is deeply embedded in the substance of the right lobe, the liver is expanded and pushed forwards as if occupied by a solid growth. When the cyst projects from the under surface of the right lobe, the liver is pushed forward, and when it protrudes beyond the lower border it may imitate an enlarged and distended gall-bladder, a tumor of kidney, uterus, or ovary, or a pancreatic cyst. A pendulous hydatid cyst may, like a distended gall-bladder, be accompanied by a linguiform lobe of the liver. A cyst growing from the anterior surface bulges the hypochondrium out, or when in the left lobe, the epigastrium forwards, in a remarkable manner. In such cases the enlargement of the liver is not uniform, as it is in cirrhosis, but is localised and may be manifestly due to a tumor, in size varying from that of an orange upwards. The hepatic enlargement does not entirely depend on the position of the cyst, though of course it is chiefly due to the presence of the cyst. When the right lobe is occupied by a large hydatid cyst, marked compensatory hypertrophy of the left lobe may occur, so that it can easily be felt to be enlarged.

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* Reichold: München. med. Wochens., April 27, 1897.

† Hillier: Trans. Path. Soc., vol. vii, p. 22.

Chauffard has recorded such a case in which the left lobe weighed almost as much as a normal liver.[*]

Usually the tumor is tense and elastic; it may, especially when thick-walled and covered by liver tissue, give the impression of a hard and solid tumor, although its contents are perfectly fluid; as has already been mentioned, the contents may in exceptional cases undergo gelatinous change, although the cyst is progressively increasing in size. On the other hand, it may occasionally fluctuate so as to imitate an abscess. On percussion the cyst is practically always dull; the entrance of air from rupture into a hollow viscus being so rare as to make it probable that in any case when the cyst appears to be resonant it is really covered by stomach or intestines. Gas has, however, been found in suppurating hydatid cysts without there being any communication with the intestinal tract, and can be explained as the result of infection with the Bacillus aërogenes capsulatus or members of the colon group.

The "hydatid thrill" is an inconstant sign and is, even when present, not pathognomonic, inasmuch as it may be obtained in other cysts. It is brought out by percussing the middle finger of the outstretched left hand when placed over the cyst; a peculiar vibration is then communicated to the contiguous fingers. This thrill was thought by Briançon[†] (1828) to be due to the impact of contained daughter cysts, but it can be obtained in sterile hydatid cysts, in tense cysts of other kinds, such as hydronephrosis, and sometimes in encysted ascites, or according to Chauffard,[‡] even in general ascites under certain conditions, such as an elastic state of the abdominal walls in young persons. The "hydatid thrill" is not very often obtained, but the conditions required for its production are more often realised in hydatid than in other cysts; so that its presence, though not absolute evidence, is strongly suggestive of the presence of a hydatid cyst. Lancereaux[§] obtained it twice in a personal experience of 60 cases; many observers have never met with it.

Hydatid cysts are rare in early life, but when they do occur, a thrill is said to be relatively less rare than in adult patients.[‖] It has been thought that the occurrence of suppuration, by altering the conditions inside a hydatid cyst, will remove the thrill (Milian[**]).

When two or more hydatid cysts are found either in or in connexion with the liver, the signs may be very confusing, and from the irregularity of the surface suggest cancer, cirrhosis with great enlargement, displacement of the liver, or affections of other organs.

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[*] Chauffard: Sem. Méd., 1896, p. 265.

[†] Briançon: Thèse, Paris, 1828.

[‡] Chauffard: Traité de Médicine, Bouchard et Brissaud, tome v, p. 303, 1902.

[§] Lancereaux: Traité des Maladies du foie et du pancreas, p. 738.

[‖] Broca: Sem. Méd., p. 89, 1901.

[**] Milian: Bull. Soc. Anat. Paris, 1900, p. 911.

In a case of multiple hydatids in the liver encroaching above on the pleural cavity the downward projection of two large cysts from the right lobe of the liver left a notch between them which during life was taken for the notch between the two lobes of the liver, the organ being thought to be displaced downwards by a pleural effusion. Two hydatid cysts in a boy aged seven projecting from the anterior surface of the right lobe gave rise to a sulcus which when felt through the abdominal walls imitated the colon passing over a tumor of the right kidney. (Cheney.[*])

Pressure on the bile-duct producing jaundice, on the portal vein inducing ascites or hæmorrhoids, or on the inferior vena cava causing œdema of the legs, is very rarely seen. Pressure symptoms are relatively less infrequent in children than in adults. Jaundice is almost constant when an hydatid ruptures into and discharges daughter cysts into the ducts, but is rare apart from this.

Stirling[†] describes a large cyst with calcareous walls springing from the under surface of the left lobe, which pressed on the common bile-duct and thus produced jaundice.

In a man who had had jaundice for eleven months and presented well-marked xanthelasma multiplex W. Legg[‡] found three hydatid cysts in the liver; one of these projected into the portal fissure and completely obliterated the common hepatic duct.

A large cyst may in rare cases compress the inferior vena cava and produce œdema of the lower limbs and the trunk, and a plexus of dilated veins over the abdomen, but complete obliteration of the inferior vena cava has been recorded without any œdema of the feet (Dévé[§]). A pendulous cyst is rather more likely to exert pressure on the inferior vena cava or right iliac veins than an ordinary hydatid cyst embedded in the substance of the liver. Ascites is practically always due to some complication; thus it occurs when there is leakage of the cyst after aspiration or spontaneous rupture. When suppuration has supervened in the cyst ascites may be due to concomitant local peritonitis. The large size of some cysts naturally leads to considerable displacement of neighbouring viscera. The amount of displacement depends on the size and situation of the cyst. The diaphragm is very frequently pushed up on the right side, and with a large cyst involving both lobes of the liver both sides of the thorax may be greatly encroached upon. In such cases or when the cyst is in the left lobe the heart may be greatly displaced upwards. As a remarkable example, reference may be made to Knaggs'[‖] case, in which the cardiac dulness was in the first and second intercostal spaces. A large cyst may displace the stomach and the other abdominal viscera. Occasionally urticaria may be the first indication of an hydatid cyst, and may be seen in a case without any proof that the cyst has ruptured or leaked. McMurray[**] records a case where pruritus and a papular rash existed for two years and disappeared the day after an unruptured hydatid cyst was removed. It has been thought that urticaria is relatively less rare in children than in adults affected with hydatid disease.

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[*] Cheney: Archives of Pediatrics, Nov., 1897, p. 651.

[†] Stirling: Intercolonial Med. Journal of Australasia, Feb. 20, 1899.

[‡] Legg, W.: Trans. Path. Soc., vol. xxv, p. 155.

[§] Dévé: Bull. Soc. Anat. Paris, 1903, p. 197.

[‖] Knaggs: Trans. Clin. Soc., vol. xxiii, p. 173.

[**] McMurray: The Australian Medical Gaz., May, 1896.

As a rule, there is no change in the blood, but in some isolated cases an increase in the proportion of eosinophile cells has been recorded. (Mimmi,* Tuffier, Neusser, Seligmann and Dudgeon,† Achard,‡ Dargein and Tribondeau.§) In some cases eosinophilia has been slight in degree and it is most exceptional to get such a high count as in Seligmann and Dudgeon's case, where the percentage was 57 and fell after the cysts were evacuated. Eosinophilia has been thought to bear a very definite relation to the presence of animal parasites in the body (Milian ‖) and to play a part in protecting against toxines manufactured by the parasites (Gulland **). If this is so, eosinophilia would occur only when absorption of the contents of a hydatid cyst is going on. Eosinophilia is by no means constant, and though its presence is in favour of a doubtful tumor being hydatid in nature, its absence cannot be held to exclude this diagnosis.

The urine is nearly always normal unless there is some complication. A suppurating hydatid may by septic absorption lead to albuminuria or conceivably to albumosuria. The mechanical effects of a large hydatid may, by pressing on the right renal veins, lead to temporary albuminuria.

Prætorius †† mentions a case where albuminuria disappeared after incision and drainage of a hydatid cyst of the liver.

In very rare cases pressure on the inferior vena cava or on the renal veins has been thought to explain great diminution in the excretion of urine. Davis ‡‡ has given an account of a woman in whom this sequence of events was thought to have occurred.

As an interesting observation Girard's §§ case of clubbed fingers associated with hydatid of the liver without any pulmonary changes may be mentioned. It was probably an accidental coincidence.

To sum up: the physical signs of a hydatid cyst in the liver are out of proportion to the symptoms; there may be great enlargement with an absence of constitutional disturbance. The most marked clinical manifestations are produced when the cysts rupture into adjacent organs or cavities, or suppurate—complications which will be described later.

DIAGNOSIS.

The diagnostic features are the presence of a cystic tumor in the liver, which is considerably enlarged, together with a marked absence of constitutional disturbance. The diagnosis cannot be made with absolute certainty unless fragments of the cyst or hooklets have been obtained by paracentesis or as the result of rupture of the cyst into the alimentary tract or in other positions. In the absence of this criterion the diagnosis is largely one of exclusion, and will be considered in the paragraphs on the differential diagnosis.

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* Mimmi: Rev. Crit. de Clin. Med., April 6, 1901.
† Seligmann and Dudgeon: Lancet, 1902, vol. i, p. 1764.
‡ Achard: Soc. de biolog., Nov. 16, 1901.
§ Dargein et Tribondeau: Ibid.
‖ Milian: Bull. Soc. Anat. Paris, 1901, p. 323.
** Gulland: Brit. Med. Journ., 1902, vol. i, p. 831.
†† Prætorius: Berlin. klin. Wochensch., 1898, S. 312.
‡‡ Davis: Lancet, 1900, vol. ii, p. 1014.
§§ Girard: La Semaine Médicale, 1903, p. 32.

Diagnosis of a Hydatid Cyst by Examination of Fluid drawn off by an Exploratory Puncture.—Although an exploratory puncture with a fine syringe is not a proceeding which should be undertaken, inasmuch as very severe symptoms and even death may follow the escape of a small quantity of fluid into the peritoneal cavity, it is often done and a diagnosis made on the characters of the fluid withdrawn. At the present time an exploratory incision should always be made and the cyst exposed. The characteristics of hydatid fluid from a living cyst are as follows: It is colourless, slightly opalescent, and neutral in reaction, with a specific gravity of 1002 to 1010, with about 1 per cent. of solids. It contains mucin, but no albumin, small quantities of sugar, inosite, succinic acid, succinate of calcium, and sometimes traces of cholesterin, leucin, and tyrosin. It contains a considerable quantity of chloride of sodium. Scolices and hooklets are not free in the living cysts and only become detached by the operation of paracentesis or when the parasite dies. The detection of hooklets is much facilitated by centrifugalising the fluid; the scolices can be seen as small white dots by the naked eye. When the parasite dies, the fluid becomes albuminous and turbid, and a toxic body, compared to myrtilotoxin, may make its appearance. When suppuration supervenes, the percentage of albumin of course increases. The laminated membrane of the ectocyst may be discharged from a suppurating hydatid and a section under the microscope presents a characteristic and beautiful appearance.

DIFFERENTIAL DIAGNOSIS.

There are a large number of conditions, such as tumors and cysts in or close to the liver, which may imitate a hydatid cyst of the liver. A hydatid cyst may (I) project from the anterior surface of the liver; (II) be deeply seated in the substance of the organ, (III) project upwards towards the thorax, or (IV) downwards into the abdomen. The conditions which may be confused with these four varieties will now be considered seriatim.

(I) **When the cyst projects from the anterior surface** of the liver diagnosis is comparatively easy. There are, however, a number of conditions which may possibly be confused with it. *Simple cysts* of the liver, though hardly ever of such dimensions as to resemble a hydatid, cannot be accurately diagnosed until their contents or their walls are examined. In multilocular cystic disease of the liver the concomitant enlargement of the kidneys should lead to a suspicion as to the true nature of the hepatic disease. In *malignant disease* there is usually cachexia, while in hydatid the general health is good. In addition, multiple malignant growths often show umbilication, and there is generally pain, neither of which is present in uncomplicated hydatid disease. The distinction, however, between malignant disease and hydatid may sometimes be very difficult.

Thus, Sargnon* describes a case in which hydatid was diagnosed and laparotomy performed; the liver, when exposed, presented the appearance of multiple growth, and the abdomen was accordingly closed; subsequently at the autopsy the growths were found to be multiple hydatid cysts.

Cholecystitis.—As a rule, inflammation of and about the gall-bladder has no resemblance to a hydatid cyst of the liver. It is only in the presence of a great deal of inflammatory adhesions around the gall-bladder and of the tongue-shaped elongation of the right lobe that any difficulty is likely to arise. Pain is prominent in most cases of chronic cholecystitis and rare in hydatid disease.

In a woman aged fifty years who was under my care the liver was much enlarged and extremely hard, while her general condition was so good that malignant disease seemed unlikely. She was first seen as an out-patient and was recommended to come into the hospital. She returned in a week's time with a pad over the liver, having been tapped without any result by a general practitioner. Laparotomy was subsequently performed by my colleague, Mr. Warrington Haward, and a greatly thickened gall-bladder containing a large number of calculi found. The calculi was removed and the patient recovered. Microscopic examination of part of the wall of the gall-bladder removed at the operation only showed chronic inflammation.

From Conditions in the Anterior Abdominal Wall.—Suppuration in the sheath of the rectus and in the anterior abdominal wall is more superficial than a hydatid and does not move with respiration in the same way, while the skin may be red and œdematous. Suppuration in the rectus is not common, and when it does occur, is usually below the umbilicus. A hydatid in the anterior abdominal wall is small and can be made out to be distinct from the liver and not to move with it. Phantom tumors and localised spasm of the right rectus abdominis muscle disappear gradually under an anæsthetic and are resonant on percussion. Localised paralysis of the rectus over the liver has been described by Potain † as resulting from rheumatism of the vertebral joints in hysterical subjects, and in cardiac dilatation from local inflammation of the peritoneal covering of the liver; the bulging and local distension which result imitating a hydatid cyst of the liver.

(II) **When the cyst is deeply embedded in the substance of the liver,** especially in the posterior part of the right lobe of the organ, and expands and pushes the liver forwards, the diagnosis is more difficult, and must be made from a variety of conditions. *Massive carcinoma* in the substance of the liver is a rare condition, and would be accompanied by severe constitutional disturbance and cachexia, and runs a rapid course. A *large cirrhotic liver*, when pushed forwards by flatulent distension of the stomach, may be sufficiently prominent to imitate enlargement due to a deeply embedded hydatid cyst. In cirrhosis the enlargement is more uniform, affecting both lobes, while the surface is not perfectly smooth; other signs of cirrhosis may be present and the general health is not so good as in hydatid disease. *Gummatous enlargement* might imitate hydatid disease, but it is usually painful, and would probably be accompanied by a history or by other manifestations of syphilis. If any doubt exists, a course of iodide of potassium and mercury should be tried.

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* Sargnon: Lyon Médical, 1898, p. 254. † Potain: Sem. Méd., 1896, p. 209.

The *painless enlargement* of lardaceous disease, leukæmia, and cardiac affections should be readily distinguished by signs of the primary diseases and examination of the urine, blood, and heart. Enlargement of the spleen would militate against ordinary, but not against multilocular, hydatid of the liver, while it would be greatly in favour of lardaceous disease and leukæmia. The various forms of *suppuration in the liver*, such as a large tropical abscess, suppurative pylephlebitis, and cholangitis, are practically always accompanied by fever, and often by rigors, while the constitutional disturbance is very considerable. The history of residence abroad, dysentery, appendicitis, or cholelithiasis would point to suppuration. But the presence of fever and constitutional symptoms indicating septic absorption are the points of most importance. When suppuration occurs in a hydatid cyst of the liver, the condition is the same as a hepatic abscess, and it can only be diagnosed by a history of a cyst having existed in the liver for a considerable time. In *subphrenic abscess* the fever and constitutional disturbance, the history of acute onset, of symptoms pointing to gastric ulcer, and in some cases the presence of air (subphrenic pyo-pneumothorax), are sufficient to distinguish it from an ordinary hydatid cyst. A suppurating hydatid may by leakage set up a subphrenic abscess.

Aneurysm of the hepatic artery is a very rare condition, and is nearly always accompanied by pain and jaundice, and the symptoms are only likely to resemble rupture of a hydatid cyst into one of the bile-ducts. In cases where the aneurysm is sufficiently large to be felt, there would almost always be pulsation.

(III) **Hydatid Cyst Projecting Upwards into the Thorax.**—When a hydatid cyst projects from the convexity of the right lobe, or in rare instances from the upper surface of the left lobe, it may be difficult to distinguish it from a pleural effusion, since it may displace the diaphragm upwards, lead to extensive collapse of the lung and to dulness over the greater part of the right side of the chest, without producing any downward displacement of the liver. In such cases the diagnosis may only be arrived at when the contents of the cyst are seen; for example, when rupture into the lung leads to expectoration of pieces of hydatid membrane or when hooklets are found in fluid drawn off by an aspirator. Skiagraphy, by showing the upward displacement of the diaphragm on the right side and its relation to the shadow cast by the heart, is more likely to assist in arriving at a correct diagnosis than any other means short of exploration at our disposal. When a hydatid cyst gives rise to the signs of a small pleural effusion and to considerable enlargement of the liver, the diagnosis is easier; but in a case with these signs the hepatic enlargement might be due to some other cause, such as cirrhosis, and the dulness in the chest to a small effusion. The dulness due to a pleural effusion differs somewhat from that of a hydatid cyst in the liver, which displaces the diaphragm upwards. If the line of dulness is highest in the axilla and falls somewhat both towards the spine and sternum, a pleural effusion is more probable, while if there is dulness at the base behind with a rounded summit there may be a cyst in the liver. (Fowler and Godlee.*)

The diagnosis between a hydatid cyst in the upper and back part of the right lobe of the liver and one in the substance of the right lung, especially when near the base, is very difficult, as the clinical signs and symptoms are very much the same. There is said to be more cough in cases of pulmonary hydatid, and there may be a band of resonance below the dulness, corresponding to the cyst, owing to the presence of some resonant lung below the hydatid. Hæmoptysis may be an early symptom in hydatid of the lung, while it is not likely to occur with a hydatid of the liver except from extreme congestion of collapsed lung; † it is rare then, and would only occur late in the disease, when the diaphragm is displaced upwards to a marked degree, viz., to the level of the second rib or even of the clavicle. From constant pressure exerted by the cyst the diaphragm may atrophy so as to allow the hydatid to project into the pleural cavity or to communicate with the lung without any suppurative or ulcerative process.

What has been said about hydatids in the lung and the diagnosis from hydatid of the upper surface of the liver applies in the case of *hydatid of the pleural cavity*. As in the case of the lung, so here the question is more likely to arise when on the right side. Luff,‡ however, met with a case where a hydatid in the left pleura, containing six pints of fluid, gave rise to signs of hydatid of the liver with probable extension into the left pleura. It is difficult or impossible to distinguish between a hydatid between the liver and diaphragm and a cyst projecting from the convexity of the liver. In both cases the liver is depressed and the pleural cavity encroached upon. When a cyst is found between the layers of the suspensory ligament of the liver, it may have started in the superficial part of the liver and grown up out of it.

(IV) **When the cyst projects downwards into the abdomen** it is usually more readily recognised, but confusion may easily arise between it and other conditions, such as a dilated gall-bladder, renal tumor or displacement, and various other abdominal tumors. There is also the greater likelihood that cysts in this position may press upon the neighbouring viscera and thus complicate the diagnosis. A dilated gall-bladder may closely resemble a hydatid cyst hanging down from the under surface of the liver. It is usually, however, not so prominent. There may have been attacks of biliary colic or of icterus in the past; though both these symptoms may follow rupture of a cyst into the bile-ducts. A dilated gall-bladder is pear-shaped and much more readily moved about than a hydatid cyst. During a laparotomy a pendulous hydatid cyst arising near the gall-bladder may be mistaken for that viscus even by an experienced observer.

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* Fowler and Godlee: The Diseases of the Lungs, p. 478.

† Galliard: Archiv. Général. de Méd., tome clxv, p. 409, 1890.

‡ Luff, A. P.: Lancet, 1896, vol. i, p. 1134.

Hydronephrosis of the right kidney when it passes forwards towards the abdominal wall may very closely resemble a hydatid; for the colon need not necessarily lie in front of the renal tumor when the latter is large. A hydronephrosis will project much more into the loin, and examination of the urine may give a clue by being of a low specific gravity, while the occurrence of inflammation in the kidney or the transition of a hydronephrosis into a pyonephrosis would be shown by the presence of pus in the urine. The discharge of a large quantity of urine associated with disappearance of the tumor is characteristic of an intermitting hydronephrosis. A soft *renal or suprarenal* growth on the right side may imitate a hydatid cyst projecting from the right lobe of the liver.

A man aged twenty-five had a fluctuating tumor below the liver, which was at first thought to be hydatid, but puncture only brought blood away. I examined him after death in 1891, and found a large cystic endotheliomatous growth arising from the right suprarenal gland and invading the right lobe of the liver by continuity.

Renal and suprarenal growths probably move less on respiration than those connected with the liver; they will tend to bulge the loin somewhat, and a careful bimanual examination should therefore always be made. A floating kidney might give rise to difficulty in diagnosis; Potain has described a form of nephroptosis, "anteversion of the kidney," which is especially likely to resemble an hydatid of the liver unless a careful bimanual examination is insisted on.

Pancreatic and Peripancreatic Cysts.—Cysts in connexion with the pancreas or a collection of fluid in the lesser sac of the peritoneum (peripancreatic cyst) are usually more prominent towards the left, and are not likely to be confused with hydatid cysts, which are only rarely attached to the left lobe of the liver. A hydatid cyst dependent from the left lobe of the liver might imitate a pancreatic cyst. Pancreatic and other abdominal cysts and tumors should be separated from the liver by a zone of resonance, while a hydatid cyst should be continuous with it. Again, a pancreatic cyst is more deeply placed and should lie behind the stomach, while a hydatid cyst would be in front. In case of doubt the stomach should be inflated with air. In the following case a suppurating hydatid attached to the back of the left lobe of the liver imitated a pancreatic cyst:

A woman aged forty-nine, the mother of ten children, was admitted under my care at St. George's Hospital on November 30, 1901. Four months previously she suddenly had an attack of very severe pain accompanied by rigors and followed by jaundice. The attacks were repeated at intervals of about two weeks. The tumor was noticed after the first attack, and was thought to have varied in size from time to time. She was a fat woman with a large, tense tumor between the umbilicus and the ensiform cartilage; close to the latter it was dull on percussion, but elsewhere it was resonant; it could not be separated from the left lobe of the liver and did not bulge into the loin. This was important, since when asked a leading question the patient said it varied from time to time according to the amount of water, sometimes excessive, that she passed. There was no jaundice or bile in the urine. The diagnosis lay between a peripancreatic cyst, a hydronephrosis, and a hydatid cyst dependent from the left lobe of the liver. It was thought to be a peripancreatic effusion into the lesser sac of the peritoneum following pancreatitis, which possibly occurred as the result of the passage of gall-stones four months before. Accordingly on December 9 Mr. Sheild made an incision over the left linea semilunaris and came down on coils of intestines somewhat matted together; on separating them stinking pus with numerous daughter cysts swelled up from a cyst attached to the left lobe of the liver. This cavity was drained. For a time the patient did well, but the discharge was very copious and she became very weak, eventually dying on December 21. At the autopsy there was a large subphrenic abscess between the diaphragm and the right lobe of the liver. The left lobe of the liver was excavated by a suppurating hydatid cyst which passed backwards and was adherent to the anterior surface of the pancreas. The pancreas itself appeared healthy. The liver was fatty and swollen and weighed 7 pounds. Both the cystic and the common bile-ducts were much dilated, but there were no gall-stones in the gall-bladder. The spleen, 4 ounces, was healthy.

A large hydatid cyst should hardly be mistaken for *ascites* unless the cyst is so large that it actually fills the abdomen, and even then the dulness will not reach to the flanks. In any case chemical examination of fluid drawn off by a trocar will settle the question. *A large ovarian cyst* in the abdomen may resemble a pendulous hydatid cyst, especially one that has contracted secondary adhesions to the lower part of the abdomen. The history of the tumor as indicating the situation where it was first noticed, whether near the liver or the pelvis, the connexion of the tumor with the liver or with the uterus, and vaginal examination are points that may assist in making a diagnosis. An ovarian cyst under ordinary conditions will not move on respiration.

THE DURATION AND PROGNOSIS.

The time during which a hydatid cyst may remain alive and capable of active growth is very difficult to estimate. But it has been thought to be as long as twenty years, which is quite in accord with the history of the following case:

A man aged thirty-five died under the care of my colleague, Dr. Penrose, in St. George's Hospital with a large hydatid, the size of an adult's head and full of daughter cysts, in the right lobe; close to it there was a small, dried-up cyst. Nineteen years before he had been tapped, and presumably the small cyst had been then evacuated. It is highly probable that the two cysts were of the same age and due to the same infection; but even if the larger cyst was due to infection at the time of tapping the other, it must have existed for nineteen years.

The prognosis of a big hydatid cyst really largely depends on whether it is operated upon or not. If it is let alone and not operated upon, it may die, shrivel up, and give rise to no further trouble, but there is no satisfactory way of prophesying whether this will happen, and a cyst which has remained quiescent or latent may suppurate without any very manifest cause. Suppuration is a dangerous complication, and its possible incidence in the remote future must be faced in deciding not to call in surgical interference.

The size, rate of growth, and the possibility of rupture or suppuration supervening are points requiring consideration. If the cyst is sufficiently large to be diagnosed and is rapidly increasing in size, the danger of rupture taking place is sufficient to make operation desirable. When a cyst gets smaller under observation, it may be undergoing spontaneous cure, and may be left alone without any immediate prospect of danger, but it is safer to remove it, for if suppuration supervenes, the conditions are then less favourable for successful operation. The situation of the cyst makes a difference in the prognosis: if it is deeply situated and in the upper and posterior part of the right lobe, it is both more likely to encroach on the thorax and more difficult to operate upon. Another point which often cannot be determined, but which is nevertheless of importance in the prognosis, is whether there is one cyst or whether they are multiple.

If a cyst is not growing rapidly, and is therefore not interfered with, there is the possible danger of traumatic rupture of the cyst, while a cyst, though not showing signs of enlargement, may rupture into some viscus to which it has become adherent. Rupture is a complication which always affects the prognosis and gives rise to anxiety, though the gravity of the prognosis varies according to the situation of the rupture. Thus rupture into the pericardium or inferior vena cava is nearly always rapidly fatal. Dévé * has shown that death need not always occur when a cyst ruptures into the vena cava, if the cysts discharged are few and small. Rupture into the peritoneum or even into the pleura may prove fatal very rapidly, while if the patient does survive, there is danger of peritonitis or of empyema. The effects of escape of hydatid fluid into the peritoneal cavity are considered below. Traumatic rupture of a living cyst may give rise to comparatively little disturbance, but rupture of a dead cyst, the contents of which have become toxic or infected with micro-organisms, is most dangerous. Rupture into parts of the peritoneum cut off by adhesions is, of course, much less dangerous, but it may then be difficult to be sure that this has occurred. Gradual leakage into the general peritoneal cavity is not necessarily followed by such grave symptoms. Rupture into the bile-ducts is very prone to set up suppurative cholangitis, and therefore is a grave complication. Ruptures into the lungs, alimentary tract, and externally are less serious. Cyr † estimated the mortality at 90 per cent. when rupture occurred into the peritoneum, 80 per cent. into the pleura, 70 per cent. into the bile-ducts, 57 per cent. into the bronchi, 40 per cent. into the stomach, 15 per cent. into the intestines, and 3 per cent. onto the surface of the body. Suppuration, of course, is also a very grave complication and makes the outlook very gloomy.

If the cyst is operated upon, the prognosis depends on the method of operation adopted, on complications arising from the operation, while there is, further, the possibility of there being other cysts which, though latent at the time of the operation and not then attracting attention, may subsequently give rise to trouble and danger.

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* Dévé: Bull. Soc. Anat. Paris, 1903, p. 185.

† Cyr: Quoted by Hoppe-Seyler, Nothnagel's Practical Encyclopædia, Diseases of Liver, p. 802. English translation.

TREATMENT.

The treatment of hydatid cysts is essentially surgical, and consists in the evacuation or removal of the cyst. No drugs given by the mouth have any effect on the parasite. A number of different methods have been employed.

I. Simple puncture with a trocar and removal of some or all of the fluid contents of the cyst. This method, which is the oldest, has been much employed, and has naturally met with approval, as it is simple and easy to perform. After the withdrawal of the fluid the parasite, under favourable conditions, dies and the cyst shrivels up.

Tapping with a trocar or an aspirator is adapted for superficial cysts close to the abdominal wall in which there is no danger of wounding adjacent structures, such as the intestines. It should not be employed for old, thick-walled cysts or when there is any sign of suppuration in the cyst. Though in many cases cure results from simple tapping, there is an element of risk, since severe symptoms and even death have followed this simple operation. The bad effects are considered on page 410. Dieulafoy* considers that the bad effects of simple tapping are due to the cyst having only been partially evacuated, and that as a result some of the residual fluid has escaped into the peritoneal cavity; he, therefore, insists on complete evacuation of the cysts, and directs that an aspirator should be used. My own opinion is, however, that the safest procedure is to have the cyst fully exposed by a surgeon and then treated as the details of the case, thus plainly seen, show to be the proper course.

II. A modification, or rather an addition to the simple procedure of tapping, consists in the injection of antiseptic fluids into the interior of the cyst. In this method a little of the fluid is removed by means of a small puncture, and a small quantity of some fluid is then introduced with the object of killing the parasite. This method, advocated by Baccelli, has been successfully put into practice by Bókay,† who injected a solution of perchloride of mercury, 1 in 1000. Other fluids, such as ox-bile, so as to imitate what has been supposed to be one cause of spontaneous cure, iodine solution, carbolic acid, alcohol, formaline, etc., have been used with the same object. These methods are dangerous and are only mentioned to be avoided. Suppuration, or even fatal mercurial poisoning, has been recorded.

III. **Electrolysis.**—Hilton Fagge and Durham ‡ employed this method with success in 7 or 8 cases. It consisted in introducing two needles into the cyst and then passing a constant electric current through the cyst, the needles being attached to the negative pole, while the positive pole of the battery was connected with a sponge placed on the skin of the abdomen over the cyst. Electrolysis acts in the same way as simple puncture, and not, as was at first imagined, by decomposition of the fluid in the cyst.

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* Dieulafoy: Acad. de Méd., May 30, 1899.

† Bókay: Archiv f. Kinderheilk., Bd. xxiii, S. 310, 1897

‡ Medico-Chirurg. Trans., vol. liv, p. 1.

Accidents and Bad Effects following Simple Tapping.—When a hydatid cyst is tapped and the fluid is partially drawn off, some of the residual fluid not uncommonly escapes into the peritoneal cavity, and its presence may be shown by some shifting dulness and fluctuation in the flanks and lower part of the abdomen. There are usually no bad symptoms, but intense itching followed by urticaria lasting from a few hours to two days may result; sometimes peritonismus, or signs of false peritonitis, follows tapping, and in rare cases death preceded by convulsions and collapse has occurred. The fluid in a living hydatid cyst contains no albumin, no hooklets, and is not capable of producing toxic effects when injected into animals, and is therefore usually without any bad effects on the man.

Chauffard,* however, met with a most exceptional case in a man aged thirty-five years; a hydatid cyst was punctured and 10 c.c. of clear fluid drawn off; epileptic convulsions set in and death followed within twenty-five minutes from the time of puncture of the cyst. The cyst contained clear fluid which was without any poisonous action on animals, and did not contain any alkaloid.

Vidal, Kirmisson, Kornach, Martini, Maury, Boinet and Chazoulière have found that the clear fluid drawn off from a living hydatid cyst, which contains neither albumin nor hooklets, is not toxic. When the hydatid cyst dies and undergoes aseptic necrosis without the introduction of micro-organisms, its characters, both physical and physiological, become changed. The fluid becomes turbid, yellow, syrupy, contains hooklets, albumin, and a ptomaine. This toxic body is analogous to myrtilotoxin found in the livers of poisonous mussels, and gives rise to the urticaria and other symptoms sometimes manifested after the escape of hydatid fluid into the tissues. This poison has been found by Boinet and Chazoulière † to crystallize in long, silky needles. Physiologically when injected into animals it induces convulsions, loss of motor and sensory power, followed by slowing of the heart, rapid respirations, dilated pupils, fall of blood-pressure, prostration and collapse, and in larger doses death. Viron ‡ has found a toxalbumin in hydatid fluid from sheep which gives rise to acute inflammation of the tissues; this throws light on local suppuration occurring in a sinus leading to a hydatid that has been aspirated.

In a man aged twenty-three years with jaundice, dangerous collapse followed exploratory paracentesis of a hydatid cyst, and subsequently a profuse urticarial rash developed on the abdomen, legs, and extensor surfaces of the arms, and lasted for some hours (L. Humphry §). Two weeks later $\frac{1}{50}$ grain of atropine was injected in order to prevent a recurrence of these severe symptoms and paracentesis was successfully performed. The late Professor Roy injected the fluid into guinea-pigs and a dog, and marked toxic symptoms were noticed. Bryant ‖ has recorded sudden death five minutes after paracentesis of hydatid of the liver; the trocar passed through the portal vein, and it is possible that the hydatid fluid may have entered directly into the circulation.

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* Chauffard: Sem. Méd., 1896, p. 265.
† Boinet and Chazoulière: Rev. de Méd., 1898, p. 845.
‡ Viron: Archiv. de Méd. experiment. et d. anat. path., 1892, p. 136.
§ Humphry: Lancet, 1887, vol. i, p. 120.
‖ Bryant, T.: Clin. Soc. Trans., vol. xi, p. 230.

The toxic effects of hydatid fluid are probably due to the contained alkaloid, and need not be regarded as the result of the personal reaction or idiosyncrasy of the patient, as Chauffard suggests. The symptoms may be grouped under three headings: (*a*) Cutaneous—pruritus and urticaria; (*b*) Cerebrospinal—epileptiform convulsions; and (*c*) collapse and cardiac failure.

As mentioned above, a hydatid rash has in very rare instances been seen without rupture or leakage of the cyst;* usually it is due to one or other of these events. It has been produced by contact with the fluid, as in the case referred to by Achard of two individuals who suffered from urticaria after making a postmortem on a case of hydatid cyst. A trocar has also been known to wound a large branch of the portal or hepatic vein and induce fatal hæmorrhage. It may be followed by suppuration in the cyst, and thus not only is time lost, but a dangerous complication results.

Surgical Treatment.—As already pointed out, the more satisfactory method of dealing with hydatid cysts of the liver is by surgical means, the abdomen being opened and the cyst exposed. For the various methods of dealing with the cyst the reader should refer to a surgical text-book. In a few instances the whole of the cyst, including the external adventitious capsule, has been removed. Generally the incision of the cyst and the removal of the parasite and daughter cysts are performed. There are dangers connected with the operation, of course, such as hæmorrhage from veins in the capsule of the cyst, and extensive and prolonged leakage of bile due to free communications between the cyst and the larger bile-ducts. The loss of bile from a cyst, if continued, may lead to emaciation if it is so extensive that all or nearly all the bile escapes from the body by this channel. This result need not occur if a fair proportion of the bile enters the duodenum. As a possible danger due to the operation, long-continued suppuration leading to lardaceous disease may be mentioned, but is much less likely to occur at the present day than in former times.

Prophylaxis.—Raw vegetables ought to be carefully washed, so as to prevent the possibility of ova being conveyed by them. As the ova are almost entirely derived from the fæces of dogs, care must be taken by those who keep dogs in the house. In places where hydatid disease is frequent, drinking-water, one of the chief means by which the disease is spread, should be filtered or boiled, while fruit and vegetables should not be eaten unless boiled or washed with filtered or boiled water.

A most necessary measure to prevent infection of dogs is burning the offal of sheep and oxen infected with hydatid cysts. Legislation should make it obligatory on the officials of slaughter-houses to burn infected offal and to prevent stray dogs getting access to this source of infection. Strict measures of this kind should be employed to stamp out the disease and prevent it obtaining a foothold in countries like America, where as yet it is not widespread. An additional measure that would have a beneficial effect would be the destruction of stray and homeless dogs.

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* McMurray: Australian Med. Gaz., May, 1896.

COMPLICATIONS.

The chief complications are rupture and suppuration of the cyst.

Rupture may occur into the peritoneum, into adjacent hollow viscera, or may perforate the diaphragm and open into the pleura, lung, or pericardium. In order to open into the serous cavities on the other side of the diaphragm the cyst must first become adherent to the under surface of the diaphragm and then penetrate the muscular and serous coats, just as a cyst has to work its way through the coats of the stomach or intestine and rupture into those organs. The process of perforation depends on atrophy, from constant pressure of the tissues of the diaphragm or intestine, which have become adherent to the cyst by local adhesive peritonitis. When suppuration has occurred, perforation and rupture occur much more readily, and in rare instances a suppurating cyst may perforate the skin of the abdominal wall.

Rupture into the peritoneal cavity may be divided into two categories:

(*a*) Into the general peritoneal cavity; the cyst may rupture freely or merely leak.

(*b*) Rupture into a localised part of the abdominal cavity which has been cut off by previous local peritonitis. A localised or subphrenic abscess may thus result.

Rupture of a hydatid cyst into the peritoneal cavity apart from traumatism or suppuration is rare, and, as already pointed out, is more readily produced in a suppurating cyst than in one that is in its ordinary condition. A hydatid cyst which is not suppurating may rupture as the result of direct or indirect violence, or even spontaneously without any manifest cause. It has been known to occur in pregnancy and may possibly be precipitated by increased intra-abdominal pressure. Usually, however, there is a history of a blow on the abdomen immediately preceding the onset of symptoms of pain and collapse.

The escape of hydatid fluid into the general cavity of the peritoneum may be rapidly followed either (i) by very severe symptoms of collapse succeeded by fatal syncope or by peritonitis, or (ii) by comparatively trivial symptoms. The factor which determines whether severe or comparatively trivial symptoms follow the escape of hydatid fluid into the peritoneal cavity is probably the state of the cyst and its contents. If the parasite is dead, the fluid becomes toxic, while the fluid from a living cyst is not toxic. Rupture of a suppurating cyst, or of one in connexion with an infected bile-duct, into the peritoneal cavity naturally sets up acute peritonitis. The sudden acute symptoms might, in the event of the presence of a hydatid cyst in the abdomen being unknown, be mistaken for irritant poisoning or perforation of an abdominal viscus. In the absence of an urticarial rash the real nature of the condition would probably only appear when the abdomen was opened. The following case illustrates the occurrence of death from peritonitis and the danger that attaches to postponing operative interference:

A woman aged thirty-four had a swelling in the upper part of the abdomen for thirteen years; it began in the epigastrium and gradually enlarged. She was admitted into St. George's Hospital on October 19, 1893, and a large hydatid was diagnosed. Operation was advised, but she was alarmed and left the hospital, only to return five days later in a state of collapse with urticaria; the tumor could no longer be felt. Mr. Turner performed laparotomy and found a ruptured hydatid cyst which entirely replaced the left lobe of the liver. The patient died next day. There was general peritonitis. No other hydatid cysts were found in the viscera.

The leakage of a cyst into the peritoneal cavity may give rise to collapse and symptoms suggesting intestinal obstruction.

This condition of "peritonismus" was well shown in a man aged thirty years under my care, who was operated upon for the symptoms of peritonitis by my colleague, Mr. Sheild, and was found to have a leaking hydatid cyst of the liver.

Rupture into the general peritoneal cavity is accompanied by sudden pain, but if the contents are not toxic or infective, recovery may follow with or without the significant, but comparatively trivial, incident of an urticarial eruption. (*Vide* p. 410.) If the cyst is large, there may be signs of ascites for some time after its rupture. This ascites may be considerable and even reaccumulate after tapping. Debove and Soupault * described such a case where tuberculous peritonitis was diagnosed.

The rupture of a hydatid cyst into the cavity of the peritoneum may be complicated by the escape of bile into the abdominal cavity (choleperitoneum). The communication of the hydatid cyst with the bile-duct may take place before or after the rupture of the cyst into the peritoneum; Dévé † believes that the latter is most often the case and compares it with the escape of bile into a cyst after tapping. The effusion of bile does not necessarily give rise to peritonitis. In cases where the bile is sterile and there is no peritonitis, the abdomen gradually swells, and after days or weeks requires tapping; the effusion has a great tendency to recur. It is curious that there is no jaundice, for the peritoneum has great powers of absorbing fluid and the quantity of bile in these cases is often very considerable.

Two after or remote effects of rupture of a hydatid cyst into the cavity of the peritoneum are: (I) Secondary infection of the peritoneum with daughter cysts; and (II) echinococcal pseudo-tuberculosis of the peritoneum.

Secondary infection of the peritoneum with numerous daughter cysts may eventually give rise to very considerable trouble. Doubt has been thrown on the secondary infection of the peritoneum with daughter cysts from rupture of a hydatid cyst of the liver, and it has been suggested that what appear to be secondary implantations are really independent cysts,‡ but this is not in accordance with the clinical facts that some years after rupture of a hydatid cyst in the liver other cysts may be found scattered over the peritoneum. The favourite situations for these secondary cysts are the great omentum and the pelvis. It probably takes about two years for the cysts to develop sufficiently to give rise to signs or symptoms. It is a somewhat remarkable fact that secondary infection of the peritoneum with daughter cysts may occur in cases where the original cyst has been in communication with a bile-duct and the daughter cysts exposed to the action of the bile.

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* Debove et Soupault: Bull. et Mem. Soc. Méd. des Hôp., 1892, p. 855.
† Dévé: Rev. de Chirurg., July, 1902, p. 67.
‡ Potherat: Bull. et Mem. Soc. de Chirurg., 1900.

Dévé* has seen secondary cysts develop in the peritoneum in cases where there was a bile-stained peritoneal effusion due to rupture of a hydatid cyst, already in communication with a bile-duct, into the peritoneal cavity. He found that scolices still continued to grow in a mixture of equal parts of hydatid fluid and bile.

Pseudo-tuberculosis of the peritoneum † after rupture or leakage of a hydatid cyst is a rarely recognised though interesting condition. It consists in small granulomata covered over by the endothelium of the peritoneum and containing pieces of hydatid membrane or hooklets. Histologically there are giant, endothelioid, and small round cells. The process may be regarded as an attempt to absorb the bits of membrane and the hooklets.

Rupture into the Pleura.—This is naturally more often seen on the right side. The effusions into the pleura may be clear or may become purulent; in the latter case the pleural cavity may be much like a large suppurating hydatid cyst with numerous daughter cysts floating in it. Such an empyema may burst into the lung. In one case under my notice where this occurred the patient was suffocated. If, as fortunately usually happens, the patient survives the rupture, a pyopneumothorax or a bronchobiliary fistula may result. Rupture of a hydatid cyst into the pleura may lead to an extravasation of bile into the pleural cavity. Dévé ‡ quotes two such cases recorded by Cruveilhier and Douart.

Rupture into the Lung.—If the lower part of the pleural cavity is obliterated by adhesions and the cyst perforates the diaphragm, rupture into the lung may follow and set up a pneumonic or even a gangrenous condition in the neighbourhood. The hydatid fluid may pass into the lung and give rise to serious dyspnœa, and hydatid membranes, which may be bile-stained, may be coughed up. Impaction of the membranes or daughter cysts in the bronchi or trachea may give rise to suffocative dyspnœa. When a hydatid cyst freely communicates with a bronchus, bile may pass into the lung and a broncho-biliary fistula may result. Out of 35 cases of broncho-biliary fistula collected by Graham,§ 11 were due to hydatid cysts of the liver. These fistulous communications between the lung and hydatid cysts are more likely to occur when the hydatid projects from the convexity of the liver.

Jones ‖ records a case of a suppurating hydatid of the liver that burst into a bronchus. The chest wall was incised and the cyst eventually extracted from the lung. The case was remarkable as occurring in a girl of only eight years of age; recovery followed.

Rupture into the pericardium is very rare, and is fatal either directly from shock or later from pericarditis.

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* Dévé: Soc. de biolog., Jan. 17, 1903.

† *Vide* Dévé: Rev. de chirurg., July, 1902, p. 79.

‡ Dévé: Rev. de chirurg., July, 1902, p. 67.

§ Graham, J. E.: Trans. Association American Physicians, vol. xii, p. 247.

‖ Jones: Lancet, 1899, vol. ii, p. 1435

Rupture into the Bile-ducts.—The frequency with which this occurs is difficult to estimate, for it often gives rise to no clinical manifestations, or may be mistaken for biliary colic due to gall-stones. In cases where the communication between the cyst and the bile-duct is small, the fluid in the cyst may run quietly away and the cyst may shrivel up; on the other hand, the cyst may be infected from the bile-duct and suppurate. The characteristic cases are those in which the communication between the cyst and the duct is sufficiently large to allow daughter cysts to escape into the duct and pass along its lumen. This gives rise to biliary obstruction, jaundice, colic, and may easily be regarded as due to gall-stones. In some cases there is fever from infective or suppurative cholangitis. In rare cases fragments of cysts or hooklets have been found in the vomit, but are more often detected in the stools. The cysts may remain in the ducts and give rise to considerable biliary obstruction and dilatation of the ducts. As already mentioned, cholangitis may result; possibly the hydatid fluid may, in the first instance, irritate the mucous membrane, in virtue of toxic bodies developed in the contents of dead cysts, and set up a descending cholangitis. But in most cases cholangitis is due to microbic infection, very possibly ascending from the duodenum, which is favoured by the presence of the grape-skin-like membranes in the larger bile-ducts. Cholangitis may spread into the evacuated cyst and set up suppuration. The suppurating cyst or ducts may perforate or leak into the peritoneal cavity and give rise to acute peritonitis or a localised subphrenic abscess. The hydatid membranes may remain impacted in the common bile-duct or even in the hepatic duct of one lobe of the liver.

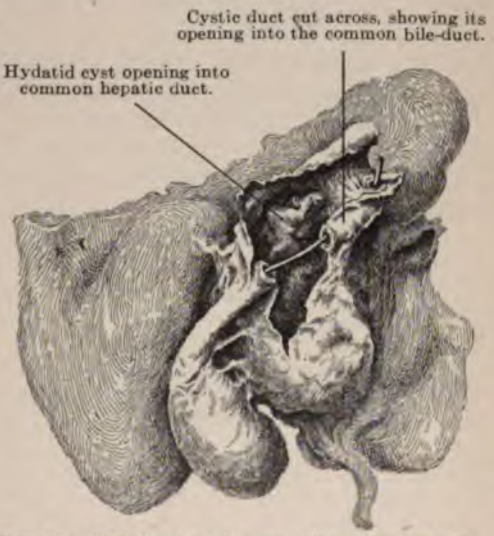
Cystic duct cut across, showing its opening into the common bile-duct.
Hydatid cyst opening into common hepatic duct.

FIG. 51.—THE COMMON HEPATIC DUCT GREATLY DILATED FROM THE PRESENCE OF PART OF A HYDATID CYST WHICH HAS RUPTURED INTO IT.

The cystic duct has been cut across so as not to obscure the view. From a specimen (Series ix, No. 196a) in St. George's Hospital Museum. (Drawn by Dr. E. A. Wilson.)

In a case under my care it seemed probable that they had for a considerable time remained in the left hepatic duct and shortly before death moved into the common duct, for the ducts in the left lobe which contained a small cyst were all dilated and suppurating, while those in the right lobe were normal.

When in the common bile-duct the membranes may project into the duodenum through the biliary papilla and pass into the intestine or they may remain in the duct. The cyst may, after rupturing into the bile-duct, perforate the diaphragm and so give rise to a broncho-biliary fistula.

Sudden death from rupture of a hydatid cyst into the left hepatic duct occurred in a man aged forty-four and was explained by Gouraud and Rathery * as due to absorption of the hydatid fluid by the intestines. This exceptional result is comparable with sudden death from rupture of a hydatid cyst into the peritoneal cavity. (*Vide* p. 412.)

The symptoms of colic followed by jaundice so strongly suggest gall-stones that the true state of affairs is not likely to be suspected unless the existence of a hydatid cyst has previously been recognised, and certainly cannot be diagnosed unless pieces of bile-stained hydatid membrane are found in the fæces or in the vomit.

Watson,† Cayley,‡ and Potain § give accounts of cases of repeated biliary colic due to the passage of hydatids.

The bile-staining of hydatid membranes is in favour of their having passed down the ducts, but this fact alone is not absolutely pathognomonic, for a cyst already in connexion with a bile-duct might discharge its contents into the stomach or bowel. When suppurative cholangitis has supervened, the underlying cause may be thought to be due to cholelithiasis, or the symptoms of fever, rigors, and jaundice might be referred to pylephlebitis, but pain and jaundice are less frequent in suppurative pylephlebitis than after rupture of a hydatid into the bile-ducts.

The following case illustrates the impossibility of diagnosing the presence of a hydatid cyst:

A man aged sixty-four was admitted into St. George's Hospital on August 11, 1897, under my care, with a history of constipation and abdominal pain for a week. No vomiting. He was slightly jaundiced, thin, and somewhat collapsed. Nothing could be felt in the abdomen, which moved freely and was flat but somewhat rigid. Left lumbar region bulged, while the right was flaccid. The temperature was not raised. A provisional diagnosis of malignant disease of colon was made; the man was, however, so bad that an exploratory operation was not considered justifiable. He died two days after admission. Postmortem examination revealed acute fibrinous peritonitis, the lymph being deeply bile-stained; the left lobe of liver contained whitish areas which resembled abscesses to the naked eye. They turned out to be dilated and suppurating bile-ducts; into the dilated bile-duct of the left lobe a thick-walled cavity lined by granulation tissue opened; all the ducts in the left lobe were dilated and showed thickening around their walls. There were no hydatid cysts in the cavity in the left lobe, but elongated hydatid skins blocked the common bile-duct. The liver was not enlarged. It seemed probable that one of the dilated suppurating ducts had ruptured or leaked into the peritoneum.

As the diagnosis is difficult and is usually made on the postmortem table, the number of reliable published cases of passage of hydatid cysts by the bile-ducts in which recovery has occurred is comparatively small. Without having gone completely into the statistics, I have notes of nine cases in which complete recovery followed. Cyr estimated the mortality at 70 per cent. It is probable that as more cases of jaundice due to obstruction of the larger ducts are now being operated upon, more examples of the collapsed cysts obstructing the bile-ducts will be forthcoming.

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* Gouraud and Rathery: Bull. Soc. Anat. Paris, 1900, p. 307.
† Watson, Sir T.: Lectures on Physic, vol. ii, p. 631, ed. v, 1871.
‡ Cayley, W.: Trans. Path. Soc., vol. xxvi, p. 127.
§ Potain: Journ. de Méd. et de chirurg. pract., Sept. 10, 1900.

Stirling * recently published a case which recovered after cholecystotomy and the subsequent discharge of hydatid membrane from the wound. The first symptom—pain like biliary colic—came on suddenly nine days before the operation, and was followed by jaundice and rigors.

In a woman aged forty, operated upon by F. T. Stewart,† the hepatic and common bile-ducts contained hydatid cysts, while the gall-bladder contained both gall-stones and free hydatid cysts. It is probable that the previous passage of gall-stones through the cystic duct had dilated the duct and thus enabled the cysts to pass out of the common hepatic duct through the cystic duct into the gall-bladder. Under ordinary conditions hydatid membranes would never be able to work their way up a normal cystic duct.

Rupture into the stomach is rare. This viscus is more likely to be penetrated when the cyst is in the left lobe of the liver. Of 11 cases referred to by Davaine, 6 were fatal. When rupture has taken place, the cyst may become tympanitic from the entry of air, and pieces of hydatid membrane, which may be bile-stained, may be recognised in the vomit or in the fæces.

Rupture into the intestines is also rare. The prognosis seems to be better than when rupture occurs into other hollow viscera, for in 15 of Davaine's ‡ cases only one died. Rupture into the duodenum is very rare, and an exact diagnosis during life is hardly possible.

In a case reported by Hale White § a hydatid in the left lobe was opened during life, the patient eventually died, and a second, suppurating, hydatid cyst was found in the right lobe. The cyst in the left lobe was found to communicate by a rather long passage with the duodenum. In a man aged twenty-six years who died jaundiced and emaciated there were two cysts, one containing bile, which was opened during life. After death a hydatid cyst of large size was found in the right lobe, which had opened into the duodenum. ‖

When rupture into the colon occurs, the prognosis would seem to be very good, since in 21 cases collected by Letanneur ** no deaths took place. On the other hand, the diagnosis of these cases, unless confirmed by an autopsy, is open to doubt; some of them may be cases of rupture into the bile-duct.††

Rupture into the inferior vena cava or the hepatic veins is very rare. In 11 cases collected by Dévé ‡‡ the cyst opened in 7 into the inferior vena cava, and in 4 into the hepatic veins. In 8 of these cases death occurred very rapidly; this may be due to cysts becoming impacted in the right side of the heart or to pulmonary embolism, the branches of the pulmonary artery being blocked with large fragments of membrane or cysts; but in some cases there is no evidence of embolism and death may have been due to toxic bodies in the hydatid fluid. Rupture into

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[*] Stirling: Intercolonial Medical Journal of Australasia, Feb. 20, 1899, p. 98.

[†] Stewart: Philadelphia Med. Journ., Sept. 2, 1899, p. 433.

[‡] Davaine: Traité des Entozoaires, Paris, 1877.

[§] Hale White: Trans. Path. Soc., vol. xxxvi, p. 252.

[‖] St. Bartholomew's Hosp. Reports, vol. xxxv, Registrar's report, p. 214.

[**] Letanneur: Quoted by Potain, Journ. de Méd. et Chirurg., Sept. 10, 1900.

[††] Compare a case recorded by F. J. Smith: Lancet, 1901, vol. i, p. 400.

[‡‡] Dévé: Bull. Soc. Anat. Paris, 1903, p. 185.

these veins need not necessarily give rise to sudden death if the daughter cysts discharged into the blood-stream are few and quite small.

There is a specimen (No. 1371) in the museum of the London Hospital of rupture of a hydatid cyst in the right lobe of the liver into the inferior vena cava.

In very rare cases (Seidel, Vegas and Cranwell[*]) fatal pulmonary embolism has been due to thrombosis of the inferior vena cava, set up by compression of the vein by a cyst. In most exceptional instances a hydatid cyst has ruptured into the pelvis of the kidney, the gall-bladder, or the portal vein. Rupture through the abdominal wall is very much rarer than in former days, as a cyst would be now treated surgically long before it had penetrated the abdominal wall. It is the most favourable place for spontaneous rupture; of 21 cases collected by Murchison, 13 recovered.

Suppuration.—Suppuration in a hydatid is a serious complication, as it practically converts the case into one of hepatic abscess. The symptoms are much the same in both cases, but in hydatid there is a marked tendency to perforate or rupture into adjacent organs or cavities; but from the fact that adhesions are less frequent around ordinary hydatid cysts, a suppurating one is not so likely to point through the skin as an ordinary hepatic abscess.

Mechanism of Suppuration in a Hydatid Cyst.—Suppuration may be set up in several ways: It may be due to direct infection from without after paracentesis or incision. It may be due to rupture of the cyst into the ducts or may follow injury to the liver, In the latter instance the resistance of the tissues around the cyst is so reduced that any micro-organisms in the neighbourhood are able to multiply and set up inflammation. Suppuration may be due to infection of the liver itself or of the bile-ducts. Petit[†] has described the spread of infection from the pleura, but in most cases of associated empyema and suppurating hydatid cysts the pleura is secondarily involved. Suppuration may occur as the result of hæmic infections; for example, in typhoid fever, infective endocarditis, and the puerperal state. When there are several cysts in the liver, suppuration may be limited to one or may extend to the others.[‡] Suppurative inflammation usually attacks a living or a dying hydatid cyst, but has occurred in one which appeared to have undergone spontaneous cure.

The results of bacteriological examination of suppurating hydatid cysts are somewhat divergent. In some instances no micro-organisms have been found, and it has been thought by Chauffard and Widal[§] that suppuration is not dependent on the presence of bacteria, but due to chemical poisons. That toxic bodies may develop in hydatid fluid is well established, and Viron[‖] has found a toxalbumin in the hydatid fluid from a sheep which set up acute inflammation. Possibly in some instances suppuration is non-microbic. In other instances micro-organisms have been isolated and in some cases mixed infections have been found. The micro-organisms observed are streptococci, Staphylococcus pyogenes aureus and citreus, pneumococcus, and Bacterium coli commune. The extremely fœtid character of the pus may depend on the presence of strictly anaërobic micro-organisms.

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[*] Quoted by Dévé: Bull. Soc. Anat. Paris, 1903, p. 196.

[†] Petit: Rev. Mens. de Méd. et de Chirurg., 1877, t. i, p. 678.

[‡] For illustrative case, *vide* Sinclair White: Brit. Med. Journ., 1897, vol. ii, p. 398.

[§] Chauffard, Widal: Soc. Méd. des Hôp., April 7, 1891.

[‖] Viron: Archiv de méd. expér. et d'anat. path., 1892, p. 136.

In a fœtid suppurating hydatid cyst in a boy aged eleven years Hallé and Bacaloglu* found, in addition to B. coli and streptococci, two strictly anaërobic microbes —Staphylococcus parvulus and Bacillus fragilis.

When suppuration takes place in a hydatid cyst, hæmorrhage not uncommonly follows, and as a result the contents have a dark purplish-red colour not unlike that seen in some cases of tropical abscess. A very rare event is the production of gas in a suppurating hydatid cyst; this is probably due to the Bacillus aërogenes capsulatus or to infection with other members of the colon group. In a case at St. Bartholomew's Hospital the presence of gas gave rise to an amphoric note on percussion over the cyst during life,† and in Habershon's‡ case there was a well-marked bell note.

A suppurating hydatid cyst by leaking may give rise to a subphrenic abscess, or exceptionally to a subphrenic pyopneumothorax.

Tuffier and Barbarin § describe the case of a woman who was operated upon for a subphrenic abscess on the right side containing air, which displaced the liver backwards. After death it was found that this depended on a suppurating hydatid cyst which had also set up general peritonitis.

For the general clinical features, etc., of suppurating hydatid cysts the reader should refer to the description of hepatic abscess.

MULTILOCULAR OR ALVEOLAR HYDATID.

History.—Cases of this rare disease were formerly regarded as examples of colloid carcinoma of the liver, until Virchow, in 1856, demonstrated their parasitic nature.

Incidence.—The disease is very rare, though possibly it is occasionally overlooked or regarded as malignant disease or multiple hydatids of the ordinary kind. It is met with in the south of Germany, Bavaria and Wurtemburg, Hannover, Switzerland, Austria, and, according to Posselt, ‖ is beginning to appear in the Tyrol. Dieulafoy ** is only able to refer to two cases of multilocular hydatid disease in France—one of the liver (Bruyant ††), the other of the lung and pleura (Rénon ‡‡). It was formerly regarded as rare in Russia, but recently 63 cases have been collected by Melnikow-Rozvedenkow,* who considers that it is more often met with there than elsewhere.

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* Hallé et Bacaloglu: Archiv de méd. expériment. et d'anat. path., Sept., 1900, p. 689.

† St. Bartholomew's Hospital Journal, Jan., 1899, p. 64.

‡ Habershon, S. H.: Practitioner, Feb., 1902, p. 178.

§ Tuffier et Barbarin: Bull. Soc. Anat. Paris, Nov., 1898, p. 689.

‖ Posselt: Deutsches Archiv f. klin. Med., Bd. lxiii, 1899.

** Dieulafoy: Manuel de Pathologie Intern., tome ii, p. 773.

†† Bruyant: Bull. hist. et scientif de l' Auvergne, 1899.

‡‡ Rénon: Soc. biolog., Feb. 12, 1900.

It is generally stated that no case has been recognised in England. There are specimens of this disease in the Army Medical Museum at Netley (Nos. 1230, 1239).

Hilton Fagge † examined a specimen of colloid cancer in the museum of Guy's Hospital which Frerichs had suggested might be alveolar hydatid, but found nothing to support this view.

In America two cases have been reported, both in natives of Germany (Osler ‡). Its geographical distribution differs from that of the common echinococcus, and it is noteworthy that it is not met with in Australia or Iceland, where the ordinary hydatid is specially common. It has been described in cows and other domesticated animals, and it has been thought that the infection is thus conveyed to man. (Posselt.)

Nature.—A good deal of discussion has taken place as to the nature of multilocular or alveolar hydatid disease, *i. e.*, whether it is merely an exogenous form of the ordinary echinococcus or an entirely distinct parasite. Klemm § found the ordinary tænia echinococcus in the intestine of a dog fed on the multilocular hydatid, but it is possible that the tænia was present in the dog previously; for Mangold, ‖ and subsequently Müller,** by giving the scolices to animals, obtained a tænia different from that of the ordinary echinococcus. The geographical distribution of the two forms does not correspond, as it should do, on the supposition that multilocular hydatid is merely the result of exogenous multiplication of the ordinary echinococcus. Melnikow-Rozvedenkow, from careful and exhaustive researches, comes to the conclusion that the alveolar hydatid is quite distinct from the ordinary echinococcal cyst. According to his views, it should be regarded as belonging to the class of the infective granulomata and be compared with tuberculosis, actinomycosis, and syphilis, since it manufactures a special irritative toxine which leads to inflammation followed by coagulation necrosis.

The embryo reaches the liver by the portal vein and becomes embedded in one of the portal spaces and develops into a chytinous multilocular mass which becomes encysted. The parasite produces ova which are spherical or oval, and measure from 170 to 1000 μ in diameter; an embryo encysted in the liver may produce 15 to 60 ova. In the production of ova when in the human body this cestode resembles the trematode worms, such as the liver fluke (Distomum hepaticum). The embryos, being endowed with amœboid movement, invade the tissues, set up inflammatory and degenerative changes, and may be destroyed by phagocytosis. When the embryos get into the hepatic veins, they may set up metastases in the lungs, brain, etc.

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* Melnikow-Rozvedenkow: Studien über den Echinococcus alveolaris, 1901.

† A Text-book of Medicine, by Fagge and Pye Smith, vol. ii, p. 459.

‡ Osler: Practice of Medicine, p. 375, ed. iv.

§ Klemm: Dissert., München, 1883.

‖ Mangold: Berlin. klin. Wochen., 1892, S. 50.

** Müller: München. med. Wochen., 1893, S. 225.

As already pointed out, alveolar hydatid leads to an exogenous formation of cysts, and thus contrasts with the endogenous production of daughter cysts inside the parent cyst which characterises the ordinary echinococcus in man.

Morbid Anatomy.—The liver is enlarged and may show no external signs of disease; it may be nodular from the projection of the parasite, and from perihepatitis be adherent to the diaphragm or to surrounding parts. According to Posselt's statistics, the right lobe is affected alone in 65 per cent. of the cases, while the left lobe is exclusively involved in 10 per cent. The posterior part of the right lobe is the seat of election. The tumor is surrounded by a fibrous capsule containing an alveolar arrangement of irregular cavities, some of which are occupied by the gelatinous hydatid cysts, others by caseous, purulent, or bile-stained débris. The appearance is much like that of colloid carcinoma. The contents of degenerated cysts may eventually resemble mortar from admixture with lime salts. The liver is hard from fibrosis, which may involve more distant parts of the organ, and may grate under the knife from calcareous infiltration. Occasionally large cystic spaces may form. The bile-ducts are often compressed, and inflammation may spread to the vessels in the portal spaces and set up endophlebitis, lymphangitis, and obstruction and obliteration. The naked-eye appearances may suggest colloid carcinoma, or, from the sponge-like structure, actinomycosis.*

Histology.—The parasite shows a structureless wavy membrane with a granular endocyst. Scolices and hooklets are not always forthcoming. In the débris of older cysts calcareous granules, cholesterin, and hæmatoidin crystals may be seen. The walls of the cavities show active proliferation of the connective-tissue cells with the production of fibroblasts and giant cells; this is followed by coagulation necrosis and caseation like that seen in tuberculosis. The liver cells may show fatty change.

Clinical Features.—The disease is usually seen in persons between twenty-five and fifty years of age, and occurs rather more often in men than in women. According to Vierordt, its incidence in the sexes is in the proportion of 3 (males) to 2 (females). The onset is very gradual, and usually the first symptoms are referred to the region of the liver, and consist of pain, weight, and discomfort. On examination the liver is enlarged and feels hard and resistant and its edge firm; the surface may be smooth, or nodular when the parasite involves the capsule. In the latter event it will be tender, and pain may be set up by perihepatitis. In rare cases fluctuation and softening may be made out in the hepatic tumor.

The spleen is said to be enlarged in 90 per cent. of the cases. Jaundice is common and occurs in four-fifths of the cases. It may be the first thing noticed and tends to become deep. As a result cholæmia with multiple hæmorrhages may develop. In rare instances the jaundice intermits and varies from time to time. As jaundice may depend on obstruction inside the liver, bile may still pass into the duodenum and appear in the fæces. Ascites is much less frequent than jaundice; it may be due to pressure on the portal vein, or to chronic inflammation of the peritoneum. Œdema of the legs may occur in the late stages of the disease, and in rare instances depends on pressure on the inferior vena cava. The urine may be of low specific gravity and so copious as to imitate diabetes insipidus. In some cases there are irregular fever and excessive perspiration; in this connexion it should be remembered that tuberculosis is said to supervene in 3 per cent. of the cases. (Posselt.*) Emaciation is a late event, and thus contrasts with the course of events in malignant disease of the liver. Digestive disturbances are not uncommon, such as dyspepsia, nausea, vomiting, diarrhœa, or constipation. In some instances there is thirst or a voracious appetite, and in these cases the bodily weight may increase.

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* Compare Wynne: St. Bartholomew's Hosp. Reports, vol. xxv, p. 159.

Course and Duration.—The disease runs a very chronic course and may last as long as ten years. Death may be due to increasing weakness or to cholæmia and continued jaundice.

Diagnosis is extremely difficult, and the disease will probably be regarded as malignant until the liver is carefully examined. This mistake has been made even when the liver has been exposed by laparotomy. The slow course of the disease may arouse a suspicion as to its real nature. Removal of a fragment of the growth at a laparotomy and microscopic examination have established the diagnosis, but mere puncture is of no value. It may also be mistaken for hypertrophic biliary cirrhosis or cysts of the pancreas. If the liver is enlarged and no localised tumor is palpable, the presence of jaundice and of splenic enlargement may suggest biliary cirrhosis. But jaundice, when present in multilobular hydatid, is much deeper than in biliary cirrhosis, and the enlargement of the spleen comes on later in the course of the disease.

Prognosis.—The difficulty of diagnosis accounts for the fact that most cases are recognised after death, and that, as far as our knowledge goes, the prognosis is bad. But it is to be hoped that comparatively early operation and excision of the growth will give good results.

Treatment.—The only efficient means of treatment is excision of the affected parts of the liver, which should be undertaken as early as possible. Bruns † has successfully treated a case by excision of the parasite. Merely tapping has not been found to be successful.

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* Posselt: Deutsches Archiv f. klin. Med., 1899.

† Bruns: Bruns' Beiträge z. klin. Chirurgie, Bd. xvii.

FATTY LIVER.

Under the heading of "fatty liver" it will be convenient to consider together the changes described separately by many writers as fatty infiltration and fatty degeneration. It will be well, however, at the outset to state briefly what is meant by the two terms.

Fatty infiltration or accumulation is an exaggeration of the physiological storage of fat in the hepatic cells; thus it is normally present in young children, sometimes in healthy adults who have died suddenly from accidents, and constantly in obesity.

Fatty degeneration is a pathological production of fat at the expense of the protoplasm of the liver cells, and is the result of a retrograde metabolism.

The histological differences between the two conditions are described on page 426, but in practice they run into each other, and it is difficult to draw a hard-and-fast line between them. It is better, therefore, to speak of pathological fatty change in the liver.

Etiology.—Pathological fatty change in the liver is met with in a number of conditions which have in common the presence of toxines or poisons in the blood. Thus a fatty state of the liver cells is the most constant change found in the bodies of alcoholic persons, and experiment shows that this must be regarded as due to the effect of alcohol as a protoplasmic poison. Numerous other poisons lead to the same change, *e. g.*, phosphorus, arsenic, antimony, chloroform, iodoform, sulphuric, oxalic, carbolic, tartaric, and other acids, sulphonal.[*]

Experimentally Rosenfeld[†] finds that phloridzin gives rise to fatty change in the liver which is an infiltration and not a degeneration, as shown by the fact that if the animal is kept without food for twenty-four hours no accumulation of fat occurs in the liver.

A certain amount of fatty change is induced by numerous bacterial toxines, and may occur in typhoid fever, pneumonia, puerperal fever, cholera, diphtheria, smallpox,[‡] scarlet fever, erysipelas, and streptococcal infections.[§] Fatty change in the liver is very frequent in pulmonary tuberculosis. Louis found it in 40 out of 120 fatal cases. It is thought to be more frequent in female than in male patients. (Budd.[‖]) It is very striking to find extensive fatty change in the liver of an emaciated patient who has little or no subcutaneous fat. Frerichs[**] regarded the fatty condition of the liver as due to the absorption of fat from the subcutaneous and other parts of the body and sometimes to imperfect secretion of bile. This theory will not stand against the facts that in cases of emaciation and jaundice, as, for example, carcinoma of the head of the pancreas compressing the bile-duct, there is often no fatty change at all in the liver. The administration of fatty food and cod-liver oil can hardly account for the change, inasmuch as cod-liver oil was not used in Louis' time. (Wilson Fox.[*]) Insufficient oxidation depending on the condition of the blood cannot be an exclusive or a very essential cause, since fatty change in the liver is much less marked in emphysema, chronic bronchitis, and congenital morbus cordis than in pulmonary tuberculosis.

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[*] Taylor and Sailer: Contributions from the William Pepper Laboratory, Philadelphia, 1900, p. 120; and Garrod: Lancet, 1900, vol. ii, 1323.

[†] Rosenfeld: Zeit. f. klin. Med., Bd. xxviii, S. 256.

[‡] Arnaud: Marseille Médical, 1899, p. 39.

[§] Roger et Garnier: Rev. de Méd., t. xxi, p. 97, March, 1901.

[‖] Budd, G.: Diseases of the Liver, p. 304, ed. iii, 1857.

[**] Frerichs: Diseases of Liver, vol. i, pp. 285, 301. Translation by New Sydenham Soc.

The fatty liver in tuberculosis is at the present time referred to retrogressive or degenerative changes set up by poisons reaching the liver. Whether this is due to the tuberculous toxine alone seems doubtful.

Peron[†] found that intravenous injections of virulent cultures of tubercle bacilli lead to extensive fatty degeneration of the liver, an effect which was prevented if the cultures had previously been raised to 100° C. for five minutes; but Carriere[‡] as a result of injection of tuberculin produced cloudy swelling, vacuolation, and necrosis of the liver cells, but never any fatty or lardaceous degeneration. The latter experiments suggest that the fatty degeneration is due to the effects of toxines other than those of the tubercle bacillus, such as might result from secondary streptococcal infections.

Fatty change in the liver cells is met with in intestinal diseases, such as dysentery, diarrhœa, etc., and would therefore appear to be due to the action of poisons absorbed from the alimentary canal.

Thus in 32 cases of gastro-enteritis in children Thiemich[§] found fatty change in 23, Freeborn[‖] found a similar condition in 50 per cent. of cases of diarrhœa in children under three years of age. Freeman[**] found that in 496 cases of children dying of various diseases the liver was fatty to the naked eye in 202, or 41 per cent., and that this change was common in acute infectious disease and in disease of the alimentary tract, but rare in other chronic wasting disorders. Ménétrier[††] has described fatty liver due to a grave infection of appendicular origin.

Fatty change is also met with in grave anæmia, and is probably due to the poisons giving rise to the anæmia. It is also well marked in cases fatal from the status epilepticus (Mott[‡‡]), in diabetic coma, and in some fatal cases of acidosis after anæsthesia in children,[§§] all of which are toxic conditions.

Fatty change in the liver is frequently present in the bodies of pregnant women, and is very probably due to the diseases or morbid conditions responsible for death. It has, however, been thought that a fatty change is constant in pregnancy. During lactation fatty change occurs in the cells around the intralobular vein and has been regarded as showing that the liver manufactures fat to be utilised in the milk (Ranvier,* Sinéty †) as an internal secretion of fat.

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[*] Wilson Fox: Treatise on Diseases of the Lungs and Pleuræ, p. 620.

[†] Peron: Soc. biolog., April 23, 1898.

[‡] Carriere: Archiv Expér. et d'anat. path. Méd., Jan., 1897.

[§] Thiemich: Beitr. z. path. Anat., Bd xx, S. 179.

[‖] Freeborn: Acad. Med. New York, Jan., 1897.

[**] Freeman: Archives of Pediatrics, 1900, p. 81.

[††] Soc. Méd. d. Hôp. Paris, Oct. 30, 1903.

[‡‡] Mott: Archives of Claybury Asylum, 1899.

[§§] Brackett, Stone, and Low: Boston Med. and Surg. Jour., vol. cli, p. 2, July 2, 1904.

Fatty change is frequently found in association with other lesions of the liver, such as cirrhosis, lardaceous disease, and chronic venous engorgement. It is then due either to some poison, to impaired nutrition, or to both factors. In some instances acute fatty transformation of the liver cells occurs and proves fatal with much the same clinical manifestations as acute yellow atrophy. In some cases there is no clear evidence as to the nature of the toxic or infective cause. It has been noted after operations,‡ and has been thought to be due to iodoform, carbolic acid, chloroform, or to a combined action of toxines due to disease and of chloroform.

Morbid Anatomy.—In cases where the liver cells rapidly undergo fatty metabolism the organ is much enlarged, for example, in phosphorus poisoning, and in extreme cases a weight of as much as 12 pounds has been reached.

In 1890 a woman aged sixty-seven, who for years had been a heavy drinker and lately had consumed a bottle of whiskey a day, was admitted into St. George's Hospital deeply jaundiced, unconscious, and with scarcely audible heart sounds; the urine did not contain leucin or tyrosin. At the autopsy, which I performed, the liver weighed 10¾ pounds and floated in water; microscopically, besides very extensive fatty change, there was some apparent increase in the amount of the fibrous tissue—probably a replacement fibrosis. The heart, 16 ounces, showed fatty degeneration. The degenerative process was probably acute, though less so than in acute yellow atrophy. It is possible that such cases should be called acute yellow hypertrophy.

The enlargement affects all parts equally and the normal shape of the liver is retained, the edges becoming rounded and thicker. When the fatty change comes on slowly, enlargement is much less marked and some fatty livers are of a normal size or occasionally small. A fatty liver is usually uniformly smooth on the surface, and as seen after death, anæmic. The consistency varies, being sometimes firm, and this without any fibrosis; sometimes soft and friable.

In a boy aged three years who died as the result of poisoning from the absorption of iodoform from a wound the liver weighed 30 ounces and was remarkably firm, keeping its shape and impressions like His' model. Microscopically there was marked fatty change but no fibrosis or lardaceous disease. During life there were high temperature, delirium, and wasting.

These differences in the consistency of a fatty liver may depend on conditions preceding death, such as septic agencies leading to acute changes, or may be the result of postmortem decomposition. On section the lobules are often very distinctly mapped out so that the surface has a granular appearance exactly like that of fine cirrhosis of the monolobular type. It is often impossible to be certain as to the existence of cirrhosis or not until microscopic sections have been made. In other cases where the fatty change affects the cells of the lobules universally the cut section is uniform and has no resemblance to cirrhosis. The specific gravity of the liver is diminished and the organ may float in water. When cut into, the surface of the section may be soft and yielding, or in some instances firm. The dry blade of a knife is rendered greasy by the exuding oil when the organ is soft. If put into a flame, the fat melts, may burn in a spluttering manner, and if allowed to drop on paper, leaves an oily stain. Local hæmorrhages and focal bile-staining may be found due to extravasation, depending on fatty degeneration and rupture of these vessels. Local areas of fatty change are not uncommonly seen in the liver in cases of a septic nature; they are due to the local action of toxines produced on the spot by micro-organisms in the vessels of the liver.

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* Ranvier: Soc. de biolog. Paris, April, 1872.

† Sinéty: de l'etat des foie chez les femelles en lactation, Paris, 1873.

‡ Compare cases and remarks by L. G. Guthrie: Lancet, 1894, vol. i, pp. 193, 257; and 1903, vol. i, p. 10. Brackett, Stone, and Low, *loc. cit.*

Histologically the liver cells contain globules of fat of varying sizes which are refractive and stain black with osmic acid. The fat is found especially in the peripheral part of the lobule, but by no means exclusively there.

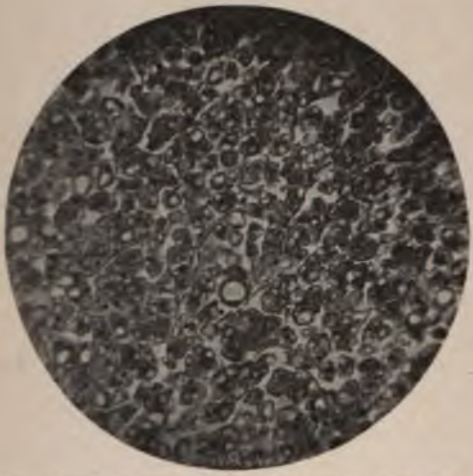


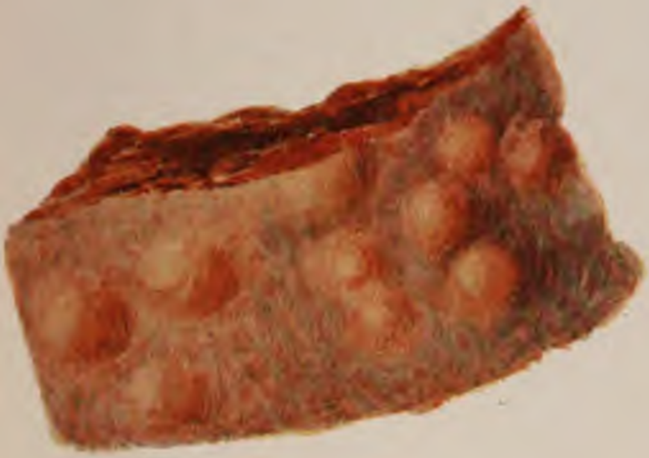
FIG. 52.—EXTENSIVE FATTY CHANGE IN THE LIVER CELLS, THE RESULT OF ACUTE DEGENERATIVE CHANGES. (Photomicrograph by S. G. Penny, Esq.)

A distinction has been drawn between fatty degeneration and fatty infiltration of the liver cells. Thus in fatty infiltration the cells at the periphery of the hepatic lobules are chiefly occupied by globules of fat of considerable size, whereas in fatty degeneration the globules are, as a rule, smaller and may occur in any part of the lobules, the process often beginning in the central zone. In fatty infiltration the protoplasm of the liver cells is mechanically displaced by the fat deposited in it, to the side of the cell, while in fatty degeneration the protoplasm is chemically altered and by retrograde metabolism has produced the fat; the cells therefore are shrunken, the protoplasm granular, and the nucleus fragmentary, but in its ordinary position. After removal of the fat in cases of infiltration the cells return to their normal state, whereas in degeneration they break up.

No hard-and-fast line can be drawn between fatty infiltration and degeneration of the liver cells; the infiltration is an exaggeration of the normal storage of fat, but it passes into a pathological condition without any corresponding and sharp distinction. Strictly speaking, fatty infiltration should concern the connective-tissue cells of the liver (Kupffer's cells)

PLATE 5.

1



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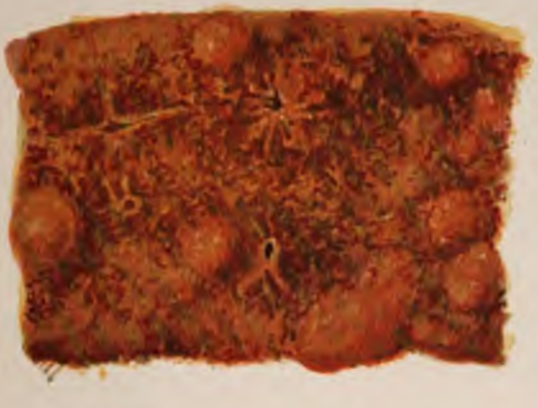

1. SURFACE OF LIVER WITH NODULAR CIRRHOSIS.

The hobnails look like masses of secondary new-growth.

2. SECTION OF THE LIVER OF ABOVE.

Showing engorgement of fibrous tissue and white colour, due to fatty degeneration of the liver cells in the hobnails. Drawn by Dr. E. A. Wilson.

and fatty degeneration the secreting cells of the liver. Although experimentally fatty change can be induced in Kupffer's cells by the injection of toxines, this is not noticeable in ordinary cases of fatty liver, whether associated with obesity or with disease. It is better to speak of fatty change in the liver rather than of fatty infiltration or degeneration.

From a review of the pathology of fatty degeneration and infiltration Herxheimer and Walker Hall * conclude that there are no reliable facts to show that fat arises directly from degeneration of the proteid molecule. The factors which lead to so-called "fatty degeneration" lower the vitality of the cells and thus favour increased deposit of fat in the cell. The term fatty degeneration should be replaced by degenerative fatty infiltration.

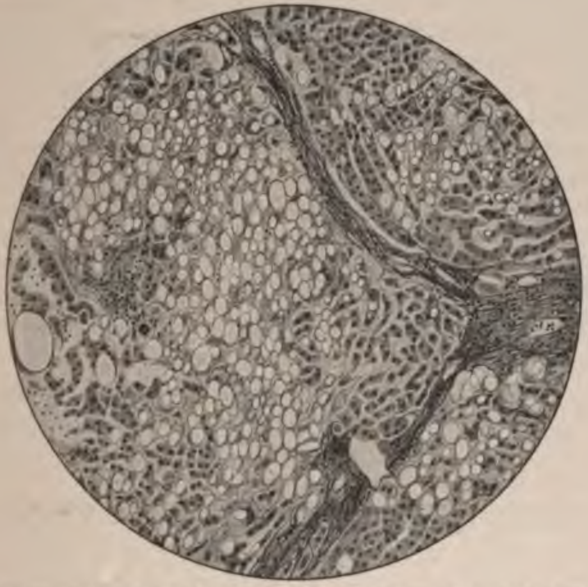

FIG. 53.—MICROSCOPIC SECTION OF LIVER, SHOWING EXTENSIVE FATTY CHANGE IN THE LIVER CELLS.

Some groups of cells are free from any change, while in others hardly any protoplasm is left. There is an increase in the amount of the interlobular fibrous tissue, suggesting slight multilobular cirrhosis. ×72.

The fibrous tissue of the portal spaces shows up so as to suggest some old fibrosis, and frequently there is some small-cell infiltration in and around the portal spaces. This is due to wasting and atrophy of the essential liver parenchyma, and may be called a "replacement fibrosis." Though in miniature much the same as hepatic cirrhosis, it is unimportant, and unless very marked, the condition should be regarded as dependent on the fatty change and should not be spoken of as fatty cirrhosis, but rather as fatty liver. In this way any confusion between this condition and genuine cirrhosis with superadded fatty change is avoided.

Clinical Picture.—*Signs.*—In cases where there is general obesity the liver may be made out by percussion to be enlarged, but it may be difficult to feel the edge distinctly, both because the abdominal walls are overloaded with fat and because during life the enlarged fatty liver is often soft. Fatty liver is indeed very often latent and unsuspected. The skin may be greasy, the tension of the pulse is usually low, and the heart sounds distant or feeble. Fat women often have remarkably small chests, and in the dead-house the contrast between the enormous fatty covering and the size of the thorax is often most striking.

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* Medical Chronicle, vol. xl, July, 1904.

In cases where a fatty liver is associated with definite disease, such as pulmonary tuberculosis, the liver is enlarged and smooth, but is less firm than in lardaceous disease or cirrhosis, and therefore not so easily felt. The spleen is not enlarged, and there is no ascites or jaundice. Addison [*] laid stress on the condition of the skin accompanying fatty liver—bloodless, looking like fine polished ivory, almost semitransparent, and exquisitely smooth, like satin. This change was earliest seen and best marked on the backs of the hands. Addison also referred to recurring attacks of œdema in cases of fatty liver, especially when the patients were alcoholic. Possibly the œdema was due to peripheral neuritis or cardiac dilatation.

The ammonia in the urine may be increased at the expense of the urea. This should be regarded not as evidence of failure in the urea-forming power of the liver cells, but as evidence that the morbid process underlying the fatty change, for example, phosphorus poisoning, leads to the formation of organic acids which seize hold of the ammonia and prevent its conversion into urea.

Lepine and Eymonnet[†] describe an excess of glycero-phosphoric acid in the urine; this is derived from lecithin, which they showed to be present in excess in fatty livers. Hæmatoporphyrinuria is often seen in cases where the liver is fatty,[‡] and may be due to the liver being unable to arrest the urobilin which reaches it from the alimentary canal.

The symptoms are those of the condition or disease responsible for the secondary change in the liver. No doubt the various functions of the liver are not so well performed as they would be if the cells were healthy, but there is no constant or preëminent failure of function. When the degeneration is very acute and at the same time extensive, the symptoms approach those of acute atrophy, although actually the liver is much larger than normal. But the condition then ceases to be one of ordinary fatty liver.

The stools are light, and the biliary secretion, though it does not fail, is probably deficient. Jaundice does not occur in uncomplicated cases, and there is no portal obstruction, so that there is no ascites or enlargement of the subcutaneous abdominal veins. Piles have been said to occur, but this is probably a coincidence. The diarrhœa formerly thought to depend on fatty liver is probably the cause rather than the effect. There is no pain associated with fatty liver.

As a result of severe traumatism fat from the liver might pass into the hepatic veins and give rise to fat embolism of the lungs. This has actually been shown to have occurred by Engel.*

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[*] Addison, T.: Guy's Hosp. Reports, vol. i, p. 476, 1836.

[†] Lepine et Eymonnet: Lyon Médical, tome xli, p. 15.

[‡] Garrod: Lancet, 1900, vol. ii, p. 1323.

Diagnosis.—Painless enlargement of the liver, with a smooth, comparatively soft surface, in an individual in whom one of the known causes of a fatty liver, such as alcoholism or pulmonary tuberculosis, is active should suggest its presence. It must be diagnosed by exclusion of the following conditions:

(1) Leukæmic infiltration of the liver leads to a firmer condition and can be at once recognised by examination of the blood.

(2) Lardaceous disease. The liver is much firmer than in fatty liver, and there may be signs of lardaceous disease of the kidneys (albuminuria), splenic enlargement, or diarrhœa.

(3) Cirrhosis, especially an enlarged cirrhotic liver with latency of the symptoms. When there are no symptoms, the diagnosis is very difficult and turns chiefly on the surface of the liver; if it is smooth, fatty change is probable, while if irregular, cirrhosis is indicated. In numerous instances fatty change is associated with cirrhosis.

(4) A displaced liver if movable is at once recognised, but if displaced by some undetected cause, such as a pleural effusion or pneumothorax, a further mistake is not improbable, and it might be regarded as a large fatty liver.

(5) Enlargement of the liver due to a deep-seated hydatid cyst or abscess. Here the liver is much more prominent and more easily felt and mapped out, while there may be signs of pressure, pain, or fever.

Prognosis.—Patients with fatty livers are very frequently addicted to chronic alcoholism, and are bad subjects for operation and bear severe illness, such as pneumonia, erysipelas, and accidents, very badly. Symonds,† Verneuil,‡ and L. Guthrie § have insisted on the danger of operations on these patients; and Guthrie, who has pointed out that chloroform narcosis is specially dangerous in patients with fatty livers, has recorded a series of cases in children in which symptoms suggesting acute yellow atrophy followed operations, and in which a fatty liver was found after death. Gilbert and Lereboullet ‖ have drawn attention to the frequency with which pneumonia proves fatal in cases where the liver is fatty, and lay stress on the view that death results in such cases not, from hepatic disease, but because of it. Apart from the dangers attending operations and acute illness the prognosis of fatty liver is that of the accompanying disease or condition.

The treatment of fatty liver is that of the primary cause, such as obesity or pulmonary tuberculosis. In cases such as those reported by Guthrie, where symptoms suggesting acute yellow atrophy came on after chloroform narcosis, the treatment is the same as in acute yellow atrophy. If there is evidence of acidosis large doses of bicarbonate of soda should be given, or it should be administered by intramuscular transfusion.

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* Engel, H.: Münchener med. Wochen., Bd. xlviii, S. 1046, 1901.

† Symonds: Med. Times and Gaz., 1860, vol. ii, p. 351.

‡ Verneuil: Gaz. des Hôp., March 3, 1881.

§ Guthrie, L.: Lancet, 1903, vol. i, p. 10.

‖ Gilbert and Lereboullet: Mem. et Bull. Soc. Méd. des Hôp., 1902, p. 577.

LARDACEOUS DISEASE OF THE LIVER.

Synonym: Amyloid, Waxy Disease of the Liver.

Hope figures an undoubted case of lardaceous disease in his work on "Morbid Anatomy" published in 1834 as "hypertrophy of the red substance of the liver." In his book on diseases of the liver in 1857 Budd[*] described the condition as "scrofulous disease of the liver."

INCIDENCE AND ETIOLOGY.

The liver is not so often affected as the spleen and kidneys. In the combined statistics of Birch-Hirschfeld, Loomis, Dickinson, Goodhart, and Turner, there are 795 cases of lardaceous disease, in which the spleen was affected 585 times, the kidney 539 times, and the liver in 387.

The causes of lardaceous change in the liver are the same as those of lardaceous disease generally, viz., prolonged suppuration and syphilis without necessarily any associated production of pus; while grave cachectic conditions due to chronic and severe toxæmias occasionally appear to be responsible for it. Tuberculosis *per se* does not give rise to the lardaceous change, but when a tuberculous lesion, for example, in the lung, or in connexion with bone, becomes secondarily infected, lardaceous disease may develop. This is seen in chronic pulmonary tuberculosis, hip-joint disease, or caries of the spine with psoas abscess.

Incidence in chronic pulmonary tuberculosis. In 326 cases tabulated by West[†] lardaceous disease was met with in 20, or 6.2 per cent.; in Wilson Fox's series of 91 cases the percentage was as high as 15.

The lardaceous change is usually produced slowly after months of suppuration, but it has been found in the liver one month after the onset of osteomyelitis (Soyka). This acute production of lardaceous change has also been produced experimentally in animals. (Krawkow,[‡] A. B. Green.[§])

Prolonged suppuration is now so comparatively infrequent that lardaceous disease is less common, and relatively more often due to syphilis, than formerly. As a result of congenital syphilis, lardaceous change is seen as a late result, but hardly ever occurs in association with the pericellular cirrhosis. In tardive hereditary syphilis it may be combined with gummata or with parasyphilitic multilobular cirrhosis. (*Vide* p. 378.) It is interesting to note that the lardaceous change may be local in the liver around a gumma, an abscess, or a suppurating hydatid. This points to the conclusion that the change is due to the action of a toxine which is derived from the abscess or gumma. Lardaceous disease is occasionally seen in other infective conditions.

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[*] Budd, G.: Diseases of the Liver, p. 312, ed. iii, 1857.

[†] West: Diseases of Respiratory Organs, vol. ii, p. 426.

[‡] Krawkow: Archiv de Méd. expérim. et d'anat. path., tome viii, 1896.

[§] Green: Journ. Path. and Bact., vol. vii, p. 184.

Comba and Malenchini* observed lardaceous change in a child, previously healthy, who died with hæmorrhagic diphtheria; in this case the change was probably due to the toxines of associated streptococci, and need not be referred, as the authors incline to do, to the diphtheria toxine.

Lardaceous change may be associated with lymphadenoma in the liver without any other cause,† and I have seen it in chronic lymphatic leukæmia.

Pathogeny.—Lardaceous change is allied to hyaline degeneration; they are different stages in degenerative modifications of protoplasm, the hyaline change being the earlier. The change consists in the production of an abnormal albuminous body and is apparently due to the action of a poison or poisons on protoplasm. This body may be produced either in the circulation or in the tissues. Czerny‡ believed that the change began in the leucocytes, since in artificial suppuration the white corpuscles when stained with iodine showed granules of a brown colour (iodophilia), which further turned to a blue colour on adding sulphuric acid. This prelardaceous substance, according to Czerny's view, passed into the tissues and became lardaceous material; according to this theory, the process is an infiltration, analogous to calcareous infiltration and not a local degeneration. Krawkow§ considered that microbic infection was absolutely necessary and that the amyloid or lardaceous change did not follow aseptic suppuration such as is set up by turpentine. He regarded the change as due to the absorption of the poisons produced by microbes, and, like Czerny, looked upon lardaceous disease as an infiltration rather than a local degeneration. These results require further confirmation.

MORBID ANATOMY.

The liver is enlarged and may weigh more than twice its normal amount; it has been known to weigh 14 pounds. The surface is smooth, usually anæmic, and may show a few stellate veins. The enlargement is uniform and the shape of the organ is so well preserved that the impressions of adjacent viscera recall His' anatomical model. The margins of the liver are firm and rounded. It is extremely firm and can be cut into thinner slices than a healthy organ. Its consistency is much increased and it is less elastic than normal, but is not so resistant to the knife as a cirrhotic liver. The specific gravity of the liver substance is higher than in health and has been said to be 1080 (Wilks ‖). The liver substance is anæmic, but its colour varies with the degree of anæmia; it may resemble the fat of bacon or, when less anæmic, look like smoked salmon. The lobular arrangement is accentuated. The glands in the portal fissure may be considerably enlarged, but do not exert pressure on the bile-ducts or portal vein. As in other organs, the lardaceous change, when slight, may not be manifest to the naked eye, and microscopic examination or staining with iodine may be necessary.

Iodine Stain.—The existence of lardaceous disease of the liver should be tested for in the postmortem room by the iodine reaction. A solution of iodine in water, containing a little iodide of potassium to dissolve it, the diluted liquor iodici of the Pharmacopœia U. S. A., or Lugol's solution (iodine 1 part, iodide of potassium 2 parts, water 200 parts), should be used. The tincture of iodine should not be employed, since the spirit it contains partially coagulates any albumin there may be on the surface of the liver and thus obscures the reaction. The cut section should first be washed to remove any blood, and since alkali interferes with the reaction, should be treated with a dilute solution of acetic acid. The solution of iodine should then be poured upon it, or, better, a thin slice of the liver should be placed in a beaker of the watery solution of iodine. The selective action of iodine is then well shown; the healthy parts are coloured yellow, while the lardaceous parts become of a dark mahogany. The intermediate zone of the lobules stands up as brown rings on a yellow ground. The colour changes if H_2SO_4 is added, but does not actually turn blue, as was originally described, but becomes a dark violet or allied tint.

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* Comba and Malenchini: Lo Sperimentale, 1901.

† Buchanan: Glasgow Med. Journ., 1889, vol. ii, p. 117. Fagge and Pye Smith's Text-book of Medicine, vol. ii, p. 647, ed. iv.

‡ Czerny: Archiv f. experiment. Patholog. u. Pharmak., Bd. xxxi, S. 209, 1893.

§ Krawkow: Centr. f. allg. Path. und path. Anat., vol. iv, p. 338.

‖ Wilks, S.: Quoted by Hilton Fagge, Principles and Practice of Medicine, vol. ii, p. 312.

Microscopic Examination.—The chief brunt of the disease falls on the capillaries in the intermediate zone of the lobules of the liver, which appear swollen, homogeneous, and tortuous. They compress and to a great extent conceal the hepatic cells, while the narrowing of the lumen of the capillaries impedes the flow of blood through them, and as a result the liver cells atrophy and degenerate. On section the swollen homogeneous curves of the capillaries imitate the appearance that would be presented by swollen hepatic cells, but the latter can be made out in appropriately stained specimens between the enlarged capillaries, and it is then seen that they never undergo lardaceous change. The lardaceous transformation of the capillaries eventually spreads throughout the lobule, and may then invade the walls of the intralobular vein. The fibrous tissue of the portal space remains healthy, as is well seen in sections stained by Van Gieson's method.

While the capillaries are the part of the hepatic vascular system chiefly attacked by the lardaceous change, examination of livers in which the change is just commencing shows that the first part to be affected is the middle coat of the small arteries; later it attacks the capillaries, and eventually, if the change is excessive, it may attack the walls of the portal and hepatic veins. When an early case of lardaceous change is examined and the change is entirely limited to the small arterioles, a condition which can be well studied around a gumma, the middle coat is seen to be irregularly affected. The lardaceous material is found to lie between the muscular fibres of the media and not in them; it spreads inwards to the intima, but neither in the arterioles nor capillaries does it involve the lining endothelium, which may be found to show fatty change.

It is noteworthy that the atrophy and degeneration of the hepatic cells are not accompanied by fibrous replacement. It is possible that this failure of reaction on the part of the connective tissue in the lardaceous liver is due to the very low state of nutrition of the fibrous tissue. (Kanthack.*) Microscopic sections may be examined fresh, with iodine solution, or preferably with methyl-aniline violet.

Staining Reactions.—With methyl-aniline violet in watery solution the lardaceous capillaries are stained red, while the healthy tissues are coloured violet; this stain is better shown if the sections are washed in water acidulated with acetic or hydrochloric acid. It is a much more delicate stain than the iodine one, and it seems probable that it reacts to an earlier stage of lardaceous change than iodine. When the lardaceous change is very far advanced, the methyl-aniline violet reaction may fail, while the iodine reaction continues to be marked. Other substances, such as colloid or hyalin, occasionally stain like lardaceous tissue. Krawkow considers that the reaction is more easily obtained in fresh sections, and that slight degrees of it may not be shown if the tissues are previously hardened. Gentian violet may also be employed; it has the same selective staining effect.

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* Kanthack, A. A.: St. Bartholomew's Hosp. Journ., Nov., 1896.

A lardaceous liver, if kept for a long time, may lose the power of staining.

Hadley* has described under the title "achroö-amyloid liver" an appearance exactly like the lardaceous change, which would not react to any of the selective stains. It does not appear that the tissues were kept for a long period before being examined; indeed, even at the autopsy the liver showed no reaction with iodine.

CLINICAL PICTURE.

Symptoms.—Lardaceous disease of the liver is usually subordinate either to the primary condition to which it is due or to the general manifestations of widespread lardaceous disease, for it is rare for the liver to be the only organ affected. There are no symptoms pathognomonic of lardaceous disease affecting the liver to the exclusion of the other viscera. Jaundice does not occur unless there is some other factor, such as a gumma. Ascites if present is in all probability due to concomitant cirrhosis, gumma, chronic peritonitis, or renal disease.

Tirard † met with œdema of legs and ascites in a child with a lardaceous liver secondary to tuberculous ostitis of the spine, but the inferior vena cava was obliterated by the spinal abscess.

Ascites does, however, occasionally occur in uncomplicated instances of lardaceous liver. It may be part of general œdema, or terminal and due to extreme cachexia. It is remarkable that although the liver is almost universally lardaceous, it shows little clinical evidence of functional inadequacy. It has, it is true, been thought that the bile is diminished in amount, and that the fæces become pale. The liver is free from pain or tenderness unless there is some complication, such as abscess, perihepatitis, growth, or gumma.

Signs.—The only real evidence of the presence of lardaceous disease of the liver is its enlargement, which is uniform, smooth, and painless. It is only when combined with gummata, cirrhosis, perihepatitis, or in the rare event of a secondary growth occurring in a previously lardaceous liver that the surface becomes rough and nodular. The left lobe of the liver may be prominent in the epigastrium and has sometimes given rise to a suspicion of primary malignant disease (Musser ‡), or been indistinguishable from an enlarged spleen.

In a case recorded by Affleck § no cause for lardaceous disease was forthcoming, and what turned out to be great enlargement of the left lobe in a lardaceous liver simulated the spleen of splenic anæmia.

DIAGNOSIS.

Under this heading the other forms of painless enlargement of the liver must be mentioned. In every case it is important to determine whether the causes for lardaceous disease are or have been present, and whether there are any signs of renal or intestinal disease of the same nature.

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* Hadley: Trans. Path. Soc., vol. l, p. 134.
† Tirard, N.: Medical Treatment, 1900, p. 338.
‡ Musser, J. H.: Philadelphia Med. Journ., May, 1899.
§ Affleck, J. O.: Edinburgh Med.-Chir. Soc., Dec. 21, 1897.

In the absence of anæmia and some degree of wasting the probabilities are against any known case of hepatic enlargement being due to the lardaceous change. In leukæmia the liver is enlarged, but a blood examination will settle any question, if such arise. When, as comparatively rarely happens, lymphadenoma attacks the liver, there will almost certainly be enlarged glands elsewhere. Simple fatty liver is less readily felt and, as a rule, is associated with obesity. In cases of phthisis an enlarged liver may be due to fatty change or to lardaceous disease, and to settle the question the other signs of lardaceous disease must be looked for; if all of them, such as albuminuria, dropsy, diarrhœa, enlarged spleen, are absent, it may be assumed that the liver is fatty.

A hydatid cyst deep in the substance of the organ may so displace the liver forwards as to imitate the physical signs of a lardaceous liver, but the other symptoms and causes of lardaceous disease are wanting, and the patient's general health is usually so good that it puts lardaceous disease out of court. A large cirrhotic liver may, from its size and firmness, imitate a lardaceous liver. In both diseases the spleen may be enlarged, and when ascites occurs in lardaceous disease, the condition may easily be regarded as cirrhosis. A history of past suppuration and the presence of albuminuria, and to a lesser degree past syphilis, are in favour of lardaceous disease, while a history of alcoholism and hæmatemesis point to cirrhosis. The following case illustrates the difficulties which may arise in correctly diagnosing between these two conditions:

A woman aged forty-seven was under my care in St. George's Hospital in June–July, 1900, with ascites, œdema of the legs, albuminuria, and signs of pulmonary tuberculosis at both apices. There was a history of hæmatemesis, and the facial aspect was that of cirrhosis. She was tapped twice and then passed into a drowsy condition from which she rallied temporarily after transfusion. At the autopsy there was lardaceous disease of the liver (53 ounces) and kidneys due to chronic phthisis. Microscopically there was no fibrosis of the liver. There was slight thickening of the capsule of the liver and opacity of the peritoneum, but not enough chronic peritonitis to account for the ascites. It is possible that the lardaceous condition of the liver, together with the slight peritoneal change, was responsible for the ascites. It is probable that what was described as hæmatemesis was in reality hæmoptysis.

PROGNOSIS.

When the liver is enlarged so that it is readily felt, and there is reason, from the history, to believe that it is due to lardaceous disease, the prognosis is bad, since the disease is likely to attack the kidneys and the intestines. The affection of the liver itself does not make so much difference, but it is evidence that the disease is present and may affect more important organs.

Under appropriate treatment a lardaceous liver may diminish in size. Sir D. Duckworth * recorded a case where it diminished by half before death occurred, and previously Graves † described great improvement

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* St. Bartholomew's Hosp. Reports, vol. x, p. 57.

† Graves: Clinical Medicine, p. 568.

in cases which were probably of the same nature. Experimentally it has been shown by Lubarsch* that lardaceous disease may pass away; he excised a piece of a lardaceous spleen from an animal some weeks before death and after death no evidence of lardaceous change was present.

TREATMENT.

The first step is to remove the primary cause of lardaceous disease, if it is still progressing. Any suppuration should if possible be submitted to surgical treatment so as to bring it to a rapid and satisfactory termination. When syphilis is the cause, iodide of potassium should be given, while good results have also been obtained from iodide of iron. If there be concomitant renal disease, the effect of iodide must be carefully watched, as an iodide eruption is then more readily produced. I have seen an eruption so produced closely resemble a uræmic rash. The general health requires careful attention and sea air, good food, and hygienic surroundings are required, while bitter tonics, iron, and acids do good. Alkalis have been recommended, chiefly on theoretical grounds, but do not succeed any better, if so well, as acids. Budd and Warburton Begbie have recommended the administration of chloride of ammonium, but its utility is very doubtful. Constipation may require attention, but mild laxatives should be given, otherwise severe diarrhœa may be set up; in fact, the treatment of constipation in tuberculous enteritis and in lardaceous disease is alike in the caution that is necessary for fear of setting up an uncontrollable diarrhœa. Diarrhœa may be very troublesome, and by exhausting the patient lead to a fatal issue. It may alternate with constipation, and should be treated by astringents, and if necessary with opium. General dropsy requires cardiac tonics, iron, and diuretics, while the skin should be made to act freely by diaphoretics and hot-air baths, or the amount of fluid should be restricted.

PIGMENTATION OF THE LIVER.

The subject of pigmentation in association with cirrhosis is described under the head of Pigmented Cirrhosis (p. 299). It is merely necessary here to mention the various conditions in which the liver cells contain pigment. The pigments may be divided into: (I) Intrinsic, or those produced in the body and derived from the blood or bile; and (II) extraneous pigments introduced into the body; these are of comparatively little importance.

INTRINSIC PIGMENTS.

These include pigments derived from the blood, viz., hæmosiderin, which contains iron; hæmatoidin, an iron-free body; and the bile pigment.

Hæmosiderin.—The cells of the liver may contain hæmosiderin—an iron-containing pigment derived from the destruction of red blood-corpuscles and the hæmoglobin thus liberated—in a number of conditions. In a systematic examination of the liver in 300 cases Castaigne† found that in 31, or more than 10 per cent., the liver cells contained hæmosiderin. This subject has been very ably dealt with by Abbott.[*] The characteristic reaction (Perl's test) for hæmosiderin consists in placing microscopic sections in a 2 per cent. solution of ferrocyanide of potassium for three minutes, transferring to a 1 per cent. solution of hydrochloric acid for two to five minutes, and washing in distilled water; the pigment granules take a bluish-green colour. This blue colouration is well seen in the cells in the periphery of the lobule in pernicious anæmia. It also occurs in leukæmia, in some cases of enteric fever, and in cases of chronic intestinal disorder. Adami[†] considers that hæmosiderin is deposited around the diplococcal form of the colon bacillus, described by him, in the liver cells. Hæmolysis of bacterial origin has been thought to account for hæmosiderosis of the liver cells in ordinary cirrhosis (*vide* p. 208) and in hæmochromatosis (*vide* p. 300). Hæmosiderosis of the liver is also seen after hæmorrhage into the peritoneal cavity, in fatal cases of purpura, and has been produced by experimental hæmolysis; for example, by toluylendiamine. (Meunier.[‡]) In some cases of new-growth in the liver the hepatic cells in the neighbourhood of the growth show hæmosiderin. I have also seen it in lymphadenoma. In malaria the liver cells may contain hæmosiderin, and it has also been described in association with suppuration. (Abbott.[§])

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* Lubarsch: Virchow's Archiv, Bd. cl, S. 471.

† Castaigne: Quoted by Chauffard, Traité de Médecine (Bouchard-Brissaud), tome v, p. 240, ed. ii, 1902.

Hæmatoidin.—This iron-free pigment is seen in and between the liver cells around the intralobular vein in chronic venous engorgement of the liver. (*Vide* p. 89.) It may also occur in the neighbourhood of hæmorrhages, innocent nævi ("melanotic angioma"), scars of old abscesses, gummata, etc.

In the various forms of biliary obstruction the liver cells are degenerated and occupied by granules of *bile pigment.*

EXTRINSIC PIGMENTATION.

In Anthracosis, Silicosis, etc.—In rather rare instances particles of carbon or of other foreign substances have been found in otherwise normal livers; the liver of cirrhosis (*vide* p. 300) may show impregnation with particles of carbon—cirrhosis anthracotica (Welch[‖]); Lancereaux[**] describes this condition in copper-workers; of stone (Adami[††]), and with silver after its medicinal use for epilepsy (Frommann[‡‡]). Reference has been made elsewhere (p. 300) to a case of cirrhosis in a sweep with pigmentation, probably due to soot, of the fibrous tissue. It is very possible that the livers of sweeps and other persons exposed to soot-laden atmospheres frequently contain soot. These conditions are interesting curiosities but have no clinical significance.

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[*] Abbott, M.: Journ. Path. and Bacteriology, vol. vii, p. 55.
[†] Adami: Journ. American Med. Assoc., Dec. 23, 1899.
[‡] Meunier: Thèse Paris, 1897–8, No. 171.
[§] Abbott, M.: Journ. of Path. and Bacteriology, vol. vii, p. 55.
[‖] Welch: Johns Hopkins Hosp. Bull., 1891, 32.
[**] Lancereaux: Traité des Maladies du foie et du pancreas, p. 380.
[††] Adami: Sajous' Annual, 1898, vol. ii, p. 313.
[‡‡] Frommann: Archiv f. Anat. u. Physiol., Berlin, 1860.

CALCIFICATION OF THE LIVER.

This condition, which is a pathological curiosity, occurs in two forms—primary and secondary.

Primary calcification is very rare; it may occur in the liver cells, as in Bristowe's and Mihel's cases or in the walls of the vessels. In three cases this calcification was associated with chronic nephritis.

In a boy aged sixteen years who died with scarlatinal dropsy Bristowe[*] found infiltration of the liver cells with an earthy salt which dissolved in acetic acid.

In a boy aged seventeen years who died from chronic pulmonary tuberculosis and parenchymatous nephritis Mihel[†] found that the liver, which grated under the knife and had the aspect of chronic venous engorgement, showed calcareous infiltration of the liver cells around the intralobular veins. The infiltration appeared to be due to calcium phosphate. In a girl aged fourteen years who died with advanced interstitial nephritis the liver was found by Brill and Libman[‡] to show calcification with calcium phosphate around the branches of the hepatic artery, which showed endarteritis obliterans. The liver showed chronic perihepatitis and chronic venous engorgement.

Babes[§] refers to a case where death occurred from tuberculous disease of the hip; the liver showed areas of calcification regarded as due to the deposit of salts absorbed from the affected bones. In a curious instance of widespread calcification affecting the heart and arteries in a man aged twenty-five years Bramwell[‖] and Gulland found the liver healthy.

Though calcification of arteries in the liver is extremely uncommon in man, it is said not to be very rare in horses; it is apparently a primary change and analogous to, if not identical with, senile calcification of the muscular coats of arteries. In the Royal College of Surgeons of England there is a Hunterian specimen of a branching piece of bone from the liver of a sheep (No. 2803), which was thought to have been formed in obliterated blood-vessels; it is probably a calcified clot in the portal vein. The occurrence of calcification more commonly in these animals is probably related to their food; thus actinomycosis in herbivora may undergo calcification, which it does not do in man.

In secondary calcification a deposit of calcareous salts occurs in inflammatory products of considerable age, such as gummata, the scars of cured abscesses, the walls of hydatid cysts, and in the walls of the gall-bladder as the result of past or chronic inflammation. A remarkable example of diffuse calcareous infiltration of the liver recorded by Targett[**] was probably secondary to syphilitic inflammation. (*Vide* Fig. 44.)

[*] Bristowe, J. S.: Trans. Path. Soc., vol. viii, p. 233.

[†] Mihel: Srpsi Arhiv za Celokupno lekarstvo., 1900. Quoted Philadelphia Med. Journal, 1901, p. 199.

[‡] Brill and Libman: Jour. Experiment. Med., vol. iv, p. 541, 1899.

[§] Babes: Virchow's Archiv, Bd. cv, S. 511.

[‖] Bramwell, B.: Edinburgh Hosp. Reports, vol. iv, p 175.

[**] Targett: Trans. Path. Soc., vol. xl, p. 123.

Carrel,* has put on record a case where a tumor of the liver due to psorospermosis underwent calcification. The tumor was removed in a laparotomy undertaken with the view that it was a calcified gall-bladder. Chemically the salts chiefly present were carbonate and phosphate of calcium.

Sometimes hard, coral-like masses, of about the size of a marble, are found embedded in the liver. They are probably the dried-up remains of biliary cysts or, in other words, intra-hepatic calculi. Small bile cysts without any general biliary obstruction are occasionally seen; as time goes on their contents become more viscid and eventually solid.

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* Carrel: Lyon Médical, tome xciii, p. 89.

LEUKÆMIC INFILTRATION OF THE LIVER.

Synonym: Leucocythæmic Infiltration.

The liver may be very greatly enlarged from leukæmic infiltration, especially in the rarer form of the disease, lymphatic leukæmia. In splenomedullary or myelogenous leukæmia there is not necessarily any enlargement, though it may be very considerable.

Murchison* describes a case which, from the illustration given of the blood, was evidently splenomedullary leukæmia, with a liver that was smaller than natural, weighing 35 ounces. On the other hand, in the two following cases of splenomedullary leukæmia examined after death at St. George's Hospital the liver was greatly enlarged. The liver of a man aged twenty-six weighed 7½ pounds, while the spleen weighed 6 pounds; both these organs showed scattered through their substance white spots resembling miliary tubercles but due to dense infiltration with leucocytes.

The liver of a woman aged twenty-seven weighed 10 pounds and the spleen 76 ounces. Together these two viscera occupied almost the whole of the front of the abdomen, a few coils of intestine only appearing above the pubes. There was no ascites. The enlargement of the liver was, contrary to what is usually seen, almost entirely of the right lobe and not of both lobes.

The liver not uncommonly weighs 5 or 6 pounds instead of 2½, and may weigh much more.

Morbid Anatomy.—The surface of the liver is pale and smooth. On section it is pale and sometimes may show naked-eye evidences of accumulations of white blood-corpuscles either in the larger portal spaces or in the substance of the liver. In rare instances there are pinkish white masses around the portal spaces; less rarely there are white spots exactly like miliary tubercles embedded in the liver substance. Microscopic examination shows that these are areas of dense leucocytic infiltration and not tuberculous granulation tissue. In the condition described as chloroma, which is really lymphatic leukæmia, the portal canals have been found to be marked out as green tracks.

Microscopically, the appearances are not always exactly alike. There may be a general and diffuse crowding of the capillaries with leucocytes with some increase at the periphery of the lobules, or there may be intense leucocytic infiltration around the portal spaces at the periphery of the lobules, with comparatively little blocking of the intralobular capillaries. When there is marked infiltration at the margin of the lobules the lobulation is clearly seen with the naked eye, and the microscopic appearances are at first sight suggestive of interlobular inflammation, *e. g.*, suppurative pylephlebitis. The leucocytes are chiefly large or small mononuclears; in splenomedullary leukæmia myelocytes are seen in the capillaries. The liver cells, especially in the centres of the lobules, may stain imperfectly from degeneration, depending on impaired nutrition, and may be fatty or atrophied. At the periphery of the lobule the hepatic cells are sometimes pigmented with hæmosiderin and resemble the appearances in pernicious anæmia. Cirrhosis does not develop as the result of leukæmic infiltration.

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* Murchison: Diseases of the Liver, ed. ii, p. 308.

Clinical Features.—There is really nothing which can be specially correlated with leukæmic infiltration of the liver in a case of leukæmia except the painless enlargement of the liver. In the latter stages of leukæmia ascites is not uncommonly present; it has been suggested that this may be due to pressure of leucocytic infiltration on the intra-hepatic branches of the portal vein, or to pressure of enlarged glands in the portal fissure in the portal vein. But it seems more probable that it is due to some concomitant chronic peritonitis and to the cardiac debility and altered blood-state. It is conceivable that ascites might be in some degree determined by thrombosis in the terminal branches of the portal vein in the liver. The urine in a case of leukæmic infiltration of the liver was found to contain hæmatoporphyrin by Garrod,* who was inclined to regard this pigment as specially related to the hepatic change. In other respects, such as the excess of uric acid, the urine shows the characters due to leukæmia.

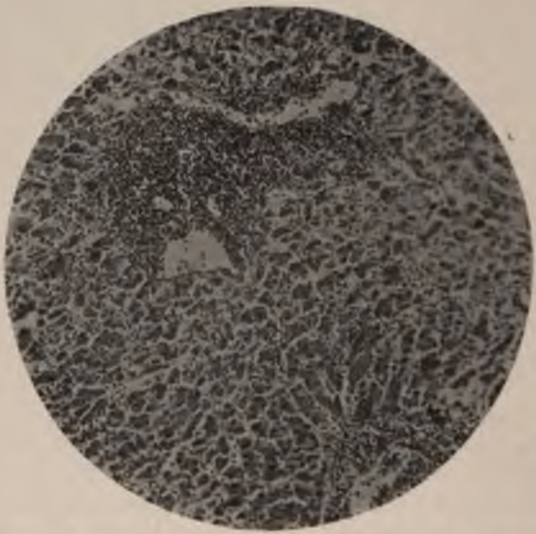

FIG. 54.—PHOTOMICROGRAPH OF LIVER IN LEUKÆMIC INFILTRATION.
There is dense leucocytic massing around a vein and an excessive number of white blood-corpuscles in the capillaries. The liver cells stain badly. (Taken by S. G. Penny, Esq.)

The **diagnosis** of leukæmic infiltration of the liver depends on an examination of the blood. This should be done in a doubtful case of painless hepatic and splenic enlargement in order to prevent the disease being regarded as lardaceous or syphilitic and treated with iodide of potassium.

The **prognosis** and **treatment** are, of course, those of leukæmia.

* Garrod, A. E.: Lancet, 1900, vol. ii, p. 1323.

SIMPLE CYSTS OF THE LIVER.

Various forms of cysts may occur in the liver, and may be conveniently classified as follows:

1. *Parasitic cysts.* Echinococcal or hydatid cysts. (*Vide* p. 389.)

2. *Cysts manifestly due to biliary obstruction.* There may be widespread dilatation of the bile-ducts in the liver in cases of long-standing biliary obstruction. The ducts stand out under the capsule and contain mucous fluid. This change is entirely secondary to the cause of the obstructive jaundice, such as carcinoma of the head of the pancreas, etc., and will not be further discussed here. The effects of biliary obstruction may be more localised and give rise to definite cysts, which in exceptional instances may be of very considerable size; in North's * case a cyst containing five pints of coffee-coloured fluid was associated with a calculus impacted in the common bile-duct.

In a man aged thirty-nine who died in St. George's Hospital with jaundice supervening in the course of pancreatic diabetes complicated with rapid pulmonary tuberculosis, there were remarkably large intra-hepatic calculi composed of bilirubin.† There were biliary cysts on the surface of the liver, with inflamed walls and fibrosis spreading outwards into the surrounding liver substance. (*Vide* Fig. 95.)

A few words may be said about *cysts occurring in cirrhosis* of the liver. They are very rare and may arise in two distinct ways: (1) By biliary retention, and then resemble those just described; (2) by the softening down of the adenomatous masses seen in nodular cirrhosis.

These cysts are small, sometimes microscopic, and are only of pathological interest. The following is an example of macroscopic cysts:

A woman aged forty-four years died with ascites and cirrhosis in St. George's Hospital. The liver, 41 ounces, was finely granular and showed microscopically multilobular cirrhosis, sometimes passing into unilobular cirrhosis. On the convexity of the right lobe near the falciform ligament there was a cyst the size of a hazel-nut with clear contents. Near it was a dried-up cyst with thick walls and almost calcareous contents. This transformation of cysts into solid formations is often seen in the kidney. The dried-up and calcareous contents of these hepatic cysts may imitate intra-hepatic calculi. This liver, which also showed the effects of tight lacing, is depicted in Fig. 6.

Microscopic cysts or dilatations of the small bile-ducts are occasionally seen.

In making microscopic sections of a hobnailed liver weighing 41 ounces, dilatation of the bile-ducts in the portal spaces was found. There was perihepatitis and chronic peritonitis in this case and small calculi in the gall-bladder, but there was no history or evidence of past biliary obstruction.

The adenomatous formations seen in nodular cirrhosis may soften down and form false cysts resembling those seen in degenerating new-growths. Cysts due to degenerative changes in carcinoma and sarcoma of the liver are described on page 489.

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* North: Medical Record (N. Y.), vol. xxii, p. 344, 1882.

† *Vide* Trans. Path. Soc., vol. xlix, p. 133.

SIMPLE CYSTS.

They are usually single or present in very small numbers; when there are a large number, the condition becomes that of cystic disease. (*Vide* p. 445.) As a rule, the cysts are small and of no clinical importance. Large simple cysts are sometimes met with. Probably some of those recorded are sterile hydatid cysts; microscopic examination of the cyst wall should decide the point. Cysts sufficiently large to contain many pints have been described.

In Bayer's* and Winckler's† cases there were thirteen and a half pints, and in North's‡ case five pints, of fluid. Doran § has written a most valuable paper on these cysts.

In some instances, such as Sharkey's, ‖ single cysts containing a pint of fluid have been found. Usually they are much smaller.

Mode of Formation.—Simple cysts are usually regarded as retention cysts due to local obstruction of the bile-ducts. Although in a fully developed stage they do not contain bile, they may do so in an early stage.

Thus in a woman aged thirty-five years who died in St. George's Hospital in 1892, with peripheral neuritis and pulmonary tuberculosis, there was a small cyst containing bile in the left lobe of the liver.

The bile disappears from the cyst probably in the same way that it does in general biliary obstruction of long standing, and becomes replaced by clear albuminous fluid. It has been suggested that a bile-containing cyst may be due to rupture of an intra-hepatic bile-duct. (Doran.) Other methods of origin have been suggested for simple cysts of the liver, such as dilatation of the glands of the larger bile-ducts or dilatation of aberrant bile-ducts. Again, some of the small single cysts with blood-stained contents may, as in the spleen, be the result of degenerative changes in nævi. A large single cyst may be due to cystic change in an adenoma of the bile-duct, the papillomatous growth softening down in the same way as adenomata of the thyroid gland.

Shattuck** reports a case in point where the cyst contained a gallon of clear fluid.

Morbid Anatomy.—The cysts are commoner on the surface of the liver than deeply embedded in its substance, but they are very seldom pedunculated; Doran refers to three large pedunculated cysts. They are usually surrounded by a firm, fibrous capsule which often contains numerous blood-vessels, and in cases of old standing may show some calcareous infiltration. In recent cysts the walls are thin. The inner surface is smooth, but is often ridged, possibly from the remains of partitions between originally separate cysts, and may resemble the inside of the auricles of the heart. It has an opaque white colour, except in cases where the cysts are very thin-walled.

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* Bayer, K.: Prag. med. Wochen., 1892, S. 637.
† Winckler: Quoted by Doran.
‡ North: Medical Record (N. Y.), vol. xxii, p. 344, 1882.
§ Doran, A.: Medico-Chirurg. Trans., vol. lxxxvii.
‖ Sharkey, S. J.: Trans. Path. Soc., vol. xxxiii, p. 168.
** Shattuck: Boston Med. and Surg. Journ., April 26, 1900, p. 427.

A typical specimen occurred in the liver of a man aged sixty-three who died of a thoracic aneurysm; on the surface of the convexity of the liver, near the falciform ligament, there was a cyst the size of a hazel-nut, with traces of partitions but not completely multilocular. In the liver of a man aged seventy-eight, who had granular kidneys with a few minute cysts, the liver, which otherwise appeared natural, contained four cysts; three of them were on the surface of the liver, the other was deeply embedded on the substance of the right lobe; it was the largest, and measured ¾ of an inch across. The contained fluid was straw-coloured and the walls were smooth.

The larger simple cysts must be distinguished from hydatid cysts by examination for hooklets and for laminated membrane, while during an operation the relations of the cyst must be noted in order to differentiate it from idiopathic dilatation of the extra-hepatic bile-ducts. The nature of the contents of these cysts varies considerably. The contents are usually clear and colourless, but may be bile- or blood-stained, green, reddish, or brown. From degenerative changes in the lining epithelium the contents may become syrupy, like some renal cysts, and so tend to dry up and form solid white encapsulated masses of small size. The fluid is albuminous and may contain blood or epithelial cells, hæmatoidin, bile pigment, cholesterin, tyrosin.* In Doran's case the cyst contained two and a half pints of bile. It is probable that as the result of injury extravasation of blood or of bile may take place into a cyst with clear serous contents.

Microscopic Appearances.—The capsule is composed of laminated fibrous tissue which may contain bile-ducts, sometimes dilated. Occasionally blood pigment is found between the bundles of fibrous tissue. The fibrous tissue invades the liver tissue for a very short distance and is lined internally by a layer of epithelial cells which may be columnar, cubical, or polyhedral in the small cysts. In exceptional instances the epithelium may be ciliated. (Friedreich,† Hanot and Gilbert.‡) In the larger cysts the cells are absent or much flattened.

Clinical Features.—Simple serous cysts are very rarely large enough to give rise to signs or symptoms. When they do, the signs are usually like those of hydatid cysts, or occasionally of an ovarian cyst, and the treatment is the same. Rupture into the peritoneal cavity may occur, and when large, induce shock and collapse. In rare instances severe hæmorrhage may occur into a large cyst and even give rise to a fatal result.

Kilvington§ mentions a case which died with symptoms like those of rupture of a large internal aneurysm, from hæmorrhage into a large simple cyst of the liver.

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* Campbell McDonnell: Lancet, 1900, vol. i, p. 453.

† Friedreich: Archiv f. path. Anat., Bd. xi, S. 466, 1857.

‡ Hanot et Gilbert: Études Sur les Maladies de foie, p. 301.

§ Kilvington: Intercolonial Medical Journ. of Australasia, vol. vii, p. 557, 1902.

In Doran's* case, where the cyst contained two and a half pints of bile-stained fluid, the patient was markedly jaundiced.

Usually simple serous cysts are found accidentally at the autopsy, and more often in middle-aged persons. Durante † has met with one in an infant in whom there was no evidence of general cystic disease of the liver.

Diagnosis.—When of such a size as to be palpable, they can only be distinguished from hydatid cysts by examination of fluid obtained from aspiration. The fluid is albuminous and does not, of course, contain hooklets.

The treatment is excision of as much of the cyst wall as is possible; this can be carried out most successfully in cases where the cyst is pedunculated. In cases where the cyst is embedded in the liver it should be dealt with on the same lines as hydatid cysts.

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[*] Doran, A.: Medico-Chirurg. Trans., vol. lxxxvii.

[†] Durante: Bull. Soc. Anat. Paris, 1902, p. 953.

CYSTIC DISEASE OF THE LIVER.

The liver may be occupied by a large number of cysts of varying sizes, and thus presents a contrast to the single or isolated cysts already referred to. This condition is spoken of as cystic disease of the liver.

Incidence.—From their age-incidence the cases may for convenience be divided into two categories—those seen in adult life and those found in the newly born; though it is very probable that those seen in adult life are also congenital, but, being less marked, have survived.

Only a few cases have been reported in *newly born infants;* there are probably not more than fifteen published cases. But it is likely that the disease is doubtless often overlooked, as it may not be manifest until the liver is examined microscopically. I have seen two cases myself, in both of which the naked-eye appearances were rather those of fibrosis than of cystic disease. As a large proportion of the cases of cystic livers in infants have been associated with deformities, such as polydactylism, etc., it is probable that if the livers of monsters and still-born children were systematically examined microscopically, congenital cystic disease of the liver would be found in a comparatively larger number.

Cases have been reported by Kanthack and myself,[*] Still (2),[†] Bar and Renon,[‡] Couvelaire,[§] Couvelaire and Porak,[‖] Carré,[**] Brindeau and Macé,[††] Kilvington.[‡‡] In all these cases the kidneys were also markedly cystic. Borst[§§] recorded a case in a child seven months old Dudgeon[‖‖] a case which was probably of this nature in a child of nine months in which the kidneys were normal; W. Müller[***] a case in a female child two years of age whose abdomen began to swell at ten months, and Batty Shaw[†††] a case in a child aged seven years in which the kidneys were not involved. These cases tend to support the view that the less marked congenital cases may persist into adult life.

Possibly the case of a full-term child the subject of many abnormalities, including cystic kidneys, obliteration of the bile-duct and communicating cysts, one in each lobe of the liver, belongs to this group; no microscopic examination, however, was made (Witzel[‡‡‡]). Gueniot's[§§§] case may also belong to this category. A full-term fœtus had 6 fingers and 6 toes, anencephaly, absence of external genitals, kidneys three times the normal size, and a cyst in each lobe of the liver; the cyst in the left lobe contained 40 grammes and that in the right lobe 80 grammes of clear fluid. This was the eighth child of a woman who married her nephew; none of the children survived; some of them showed abnormalities.

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[*] Kanthack and Rolleston: Virchow's Archiv, Bd. cxxx, S. 488.

[†] Still: Trans. Path. Soc., vol. xlix, p. 155.

[‡] Bar and Renon: C. R. Soc. de biolog., 1894, p. 835.

[§] Couvelaire: Annal de Gyn. et d'obstet., Nov., 1899.

[‖] Couvelaire and Porak: C. R. de la Soc. d'obstet. et de Gynec. et de Pediat., Paris, Jan., 1901, p. 26.

[**] Carré: Thèse Paris, 1901, No. 232.

[††] Brindeau and Macé: Gaz. Hebdom., Feb., 1899.

[‡‡] Kilvington: Intercolonial Med. Journ. of Australasia, vol. vii, p. 557, 1902.

[§§] Borst: Festschrift der phys. med. Gesellschaft, Würzburg, 1899.

[‖‖] Dudgeon, L.: Trans. Path. Soc., vol. liv, p. 296.

[***] Müller, W.: Virchow's Archiv, Bd. clxiv, S. 270.

[†††] Shaw, H. B.: Lancet, 1903, vol. i, p. 1447.

[‡‡‡] Witzel: Centralblatt f. Gynäk., 1880, S. 561.

[§§§] Gueniot: Bull. de l'Acad. de Méd. Paris, tome xxv, p. 169, 1891.

Association with Cystic Disease of the Kidneys.—Real cystic disease of the liver is practically always accompanied by a similar and almost always more advanced change in the kidneys. This association was first noted by Bristowe.* A few accidental cysts may occur in the liver without any similar change in the kidney, but this hardly constitutes cystic disease.

Two cases of probable cystic disease of the liver without similar change in the kidneys have been referred to (Dudgeon and Batty Shaw). Dr. Lazarus-Barlow has told me of a case of cystic disease of the liver in a young adult in which the kidneys were normal.

Cystic kidneys not uncommonly occur without cystic disease of the liver.

In 63 cases of cystic kidneys collected by Lezars† 46, or 73 per cent., were free from cystic change in the liver. In 90 cases of congenital cystic disease of the kidneys Luzzato‡ found five in which the liver was similarly affected. Still§ collected 35 cases of combined cystic change in the liver and kidney, of which 3 were in infants.

Concomitant cysts in other organs have been described, but it is doubtful whether any importance should be attached to the observation.

Age.—Multilobular cystic disease is usually observed comparatively late in life, apart from the rare cases seen in infants. In 26 cases collected by Still, 17 were over fifty, and 4 over seventy, years of age; the youngest adult case was thirty-nine.

Sex.—The female sex is more often affected than the male—according to Still, in the proportion of 3 to 1; 21 of his 28 cases being females.

MORBID ANATOMY.

In **congenital cystic disease** in infants the liver is in a majority of the few recorded cases little if at all enlarged, and does not present any manifest naked-eye evidence of cystic change, except perhaps a few minute cysts on the surface of the organ. In Porak and Couvelaire's ‖ remarkable case the liver was so large that it impeded delivery and had to be tapped before the fœtus, which was greatly deformed, could be extracted. On section the fibrous tissue in the portal spaces is considerably increased in amount; a few cystic dilatations may appear, but most of them are microscopic. The naked-eye appearances are usually more suggestive of fibrosis than of cystic change. The larger bile-ducts and the gall-bladder are healthy.

Probably the existence of combined cystic disease of the kidney and liver is sometimes overlooked; the kidney change is well marked, while that in the liver may, unless examined microscopically, escape detection. It is therefore desirable that the liver should always be examined microscopically in cases of cystic disease of the kidney. The contents of the cysts are clear and do not contain bile.

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* Bristowe, J. S.: Trans. Path. Soc., vol. vii, p. 229.
† Lezars: Thèse Paris, 1888.
‡ Luzzato: Quoted by Boinet and Raybaud, Rev. de Méd., Jan. 10, 1903.
§ Still, G. F.: Trans. Path. Soc., vol. xlix, p. 155.
‖ Porak and Couvelaire: Loc. cit.

In **adult cases** of cystic disease the liver may be very greatly enlarged, though this is not always the case.

A cystic liver in the College of Surgeons Museum weighed 13 pounds 7 ounces, and in Roberts'* case 11½ pounds.

A cystic liver from an adult woman may show the deformity of tight lacing. (*Vide* St. Bartholomew's Hosp. Museum, No. 2204 D.)

The degree of cystic transformation is nearly always much less in the liver than it is in the kidneys. The kidneys are usually megalocystic, while the cystic liver is smaller in proportion. The cysts are, however, bigger than those seen in babies, probably from the fact that several cysts, originally separate, have united together. Their size varies very considerably; there may be a number of quite small ones, with one or more larger ones. In cases where the liver is considerably enlarged there may be a number as big as a walnut. In exceptional instances a very large cyst may be formed.

In Cleaver's† case there were many small cysts and a single large one measuring 7½ inches in circumference.

The cysts appear on the surface of the organ and may thus give rise to considerable deformity. They are surrounded by a capsule of well-formed fibrous tissue. On section the liver is more or less honey-combed by numbers of independent cavities. The cysts usually contain clear albuminous fluid, which is sometimes brown, probably from hæmorrhage. They contain abundant proteids, urea, chlorides, and sometimes blood and epithelial cells, cholesterin, oxalate of calcium, leucin, and creatinin,‡ but not bile. There is a considerable increase in the amount of fibrous tissue in the liver. The large bile-ducts and the gall-bladder are free from any special change.

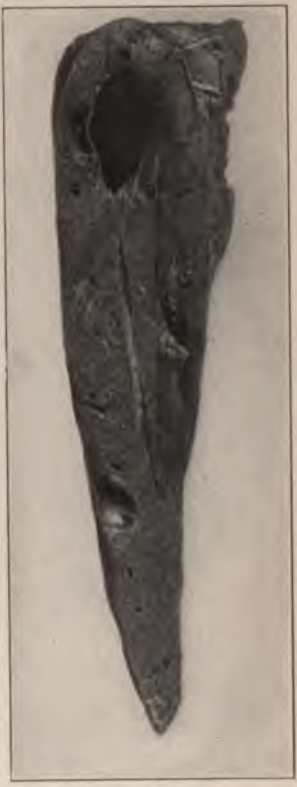

FIG. 55.—SECTION OF CYSTIC DISEASE OF THE LIVER IN AN ADULT.

The liver also showed a furrow due to tight lacing. (Photographed by Dr. H. Morley Fletcher.)

Microscopical Appearances.—In the cystic livers of newly born infants there are a number of tubules in the portal spaces which are lined with subcolumnar epithelium and are somewhat dilated. They closely resemble dilated bile-ducts, but are far more prominent and appear to be more numerous than the normal bile-ducts. They may appear completely to encircle the interlobular vein. From the portal space these dilated tubes can be traced into the interlobular tissue; they are accompanied by fairly well-formed fibrous tissue. These epithelial extensions between the lobules are at first somewhat dilated, but as they get further away from the portal space they tend to become solid cylinders, and when cut obliquely, may appear to have more than one layer of cells lining them. There are never any masses of bile in these tubes or cysts.

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* Roberts: Annals of Surgery, vol. xix, p. 251.
† Cleaver: Philadelphia Medical Journ., 1901, p. 1139.
‡ Forbes, J. G.: St. Bartholomew's Hospital Reports, vol. xxxiii, p. 207.

The fibrosis thus tends to be unilobular, with exaggerations around the larger portal canals; there is no intercellular cirrhosis and no evidence of congenital syphilis. In places blood is seen to be extravasated into the substance of the hepatic lobules. The liver cells are usually well preserved; exceptionally they have been found to show a peculiar change which at first sight might suggest fatty metamorphosis, but, as shown by the absence of staining with osmic acid, this is not the case. On the other hand, this appearance may be explained as sections of dilated biliary capillaries which, having invaginated or indented the liver cells, give the impression of being inside the cells.

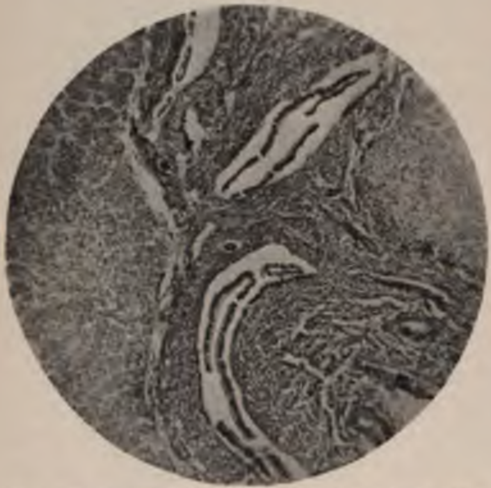

FIG. 56.—PHOTOMICROGRAPH OF CONGENITAL CYSTIC DISEASE OF THE LIVER.

Shows portal space with increased quantity of well-formed fibrous tissue and with dilated tubes lined by columnar epithelium, which has separated from the walls in the process of hardening. The hepatic cells show vacuolation. (By Dr. Harold Spitta.)

In the adult form the cysts are much larger, are surrounded by well-formed fibrous tissue, while there may be numerous blood-vessels in the immediate neighbourhood. In the smaller cysts the epithelium is columnar, in the medium-sized cysts it becomes cubical or polyhedral, and in the larger ones it is either absent or represented by a few flattened cells.

In exceptional cases ciliated epithelium has been described in the cysts.*

The bile-ducts in the liver are often dilated in parts, but this is not constant. The hepatic cells are, generally speaking, healthy, but may show the vacuolated appearance described in congenital cases.

Pye Smith† regarded this change as due to intracellular cyst formation and to be a degenerative process beginning long after adult life.

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* Lezars: Thèse Paris, 1888, p. 34. Hanot et Gilbert: Maladies du foie, p. 295.

† Pye Smith: Trans. Path. Soc., xxxii, p. 112, 1881.

A point of interest is the connexion between congenital cystic disease and the similar anatomical condition more often met with in adults. They are so similar that it appears reasonable to regard the adult cases as congenital in origin, and to explain the survival by supposing that the change in the liver and kidneys is less extensive than in those rare cases where death takes place in infancy. Still regards cystic disease of the liver as a malformation which is not progressive, and on this theory it is easy to understand that, if the subject can survive the early effects, life may be prolonged for years.

PATHOLOGY.

The causation of cystic disease of the liver has given rise to a great deal of discussion, and various theories have been put forward. It is so generally combined with similar change in the kidney that it is highly probable that whatever the causal factor is, it is the same for them both. Pye Smith, it should be noted, considers the change in the kidney and in the liver to be independent. The following theories may be referred to as bearing on the causation of cystic disease of the liver.

Inflammatory Theory.—The oldest view was that there was primary inflammation of the fibrous tissue surrounding the bile-ducts, which thus led to dilatation of the bile-ducts. (Michalovicz, Juhel, Renoy, Babinsky.) The process might be described as one of pericholangitic inflammation leading to a biliary cirrhosis of the liver with dilatation of the bile-ducts. It might perhaps be possible to explain the process as a fairly acute cholangitic and pericholangitic inflammation during fœtal life, which so weakens the walls of the small ducts that they then dilate and never recover their proper size, while the inflammatory products organise into firm fibrous tissue. Further, the inflammation might be followed by epithelial proliferation and the formation of new bile-ducts.

This explanation of the change in the liver is surrounded with difficulties. If it be regarded as biliary cirrhosis with subsequent dilatation, a form of "epithelial cirrhosis" analogous to cystic disease of the breast, the objection at once arises that in biliary and indeed in the other protean forms of cirrhosis any dilatation of the ducts is of extreme rarity.

A further objection against this view is the absence of jaundice in cystic disease of the liver both in infants and in adults, while in congenital obliteration of the bile-ducts where there is an intra-uterine inflammation of the intra-hepatic bile-ducts, practically identical with that postulated by this theory, there is persistent jaundice. The absence of jaundice is rather surprising, whatever theory is held as to the origin of the cysts, for if they are not obstructed ducts themselves, but independent formations, the real ducts should be pressed upon. This, however, can hardly occur, for there is no bile-staining of the liver itself or accumulations of inspissated bile in microscopic sections of the liver. It is noteworthy that in the rare condition of chronic pericholangitis where the bile-ducts must be compressed there is no trace of jaundice either locally in the liver or elsewhere; it is possible that in both instances this anomaly depends on the lymphatics being obstructed so that bile cannot be absorbed.

Beale[*] injected the larger bile-ducts in Bristowe's original case with Prussian blue and found that no injection passed into the cysts; from this he concluded that the formation of cysts did not depend upon closure of a part of the tube and the subsequent accumulation of secretion beyond this point. It is difficult to follow this argument, for if the cysts were due to retention, the injection would not be able to pass the obstruction and flow into the cysts. The fact that injection does not pass into the cysts does not, however, prove that the cysts are unconnected with the bile-ducts, for Barrett,[†] in experiments on normal livers, found that when the common bile-duct was injected, under pressures of from 45 to 300 mm. of mercury (the normal pressure under which bile is secreted being 20 to 45 mm. of mercury), with gelatine, none of the injection passed into the bile canaliculi.

Theory that the Cysts are a New Formation.—Rindfleisch[‡] believed the cystic change to be a cystic sarcoma starting from the bile-ducts. A number of authors have regarded the changes in the ducts as of an adenomatous nature (Nauwerck and Hufschmidt,[§] Workman,[||] v. Kahlden). Malassez[**] and Claude[††] considered that the disease was a cystic fibro-adenoma homologous to an ovarian cystadenoma. Claude regarded the cysts as dilated new bile-ducts and believed that the process had a special relation to arteriosclerosis. Sabourin,[‡‡] who has paid much attention to this subject, describes cystic disease of the liver as a cavernous biliary angioma, and regards it as due to irritation which leads to development of new bile-ducts from various sources, such as preëxisting bile canaliculi, possibly from their mucous glands or from vasa aberrantia. The ducts thus formed unite, anastomose, dilate, and lead to the formation of larger ones by the destruction and absorption of the intervening septa.

Degenerative Theories.—Pye Smith,[§§] in his case of combined cystic disease in the kidneys and liver in a man aged fifty-three, described vacuolation of the liver cells. The vacuoles began in the protoplasm, one or more occurring in the same cell; these joined, and by fusion with those formed by other cells led to the formation of cysts. This change he regarded as originating long after adult life had been reached. This appearance may be seen in congenital cystic disease of the liver. The vacuoles are probably sections of dilated bile capillaries invaginating the liver cells. Pilliet[||||] regards cystic disease as a result of atrophy of the liver in which the liver cells become changed into newly formed bile-ducts and vasa aberrantia. These tubes by dilatation give rise to the multiple cysts.

Developmental Theory.—Still has put forward with great ingenuity a theory which is on the same lines as Shattock's * view of the nature of cystic kidneys. According to the latter view, the mesonephros persists and its dilated tubules form the cysts, while the metanephros or real kidney is blended with and compressed by the fœtal persistence. In the case of the liver, Still † supposes that some of the columns of hypoblastic cells forming part of the original duodenal diverticulum develop irregularly and form the cystic tubes, while the bile-ducts proper develop in the ordinary way and can be seen in the portal spaces. The excess of fibrous tissue he regards as a persistence of fœtal mesoblastic stroma and not inflammatory. In other words, the change is a malformation, and is therefore not necessarily progressive. Hence if death does not happen to occur in early life, the cystic change may be found as a persistent condition in the adult cases. The close association with cystic kidneys, also, according to Shattock's view, a malformation, is thus rendered intelligible. It is also significant that other malformations may coëxist. Thus in one case the remarkable association of polydactylism, occipital meningocele, and webbed toes was found; in another a misplaced kidney; in another an undescended testis;‡ and in several more polydactylism. These external malformations are not met with in adult cases, and are not constant in the cases fatal at birth. It may reasonably be supposed that the cases in which the developmental defects are comparatively slightly marked persist to adult life.

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[*] Beale, L.: Trans. Path. Soc., vol. vii, p. 234.

[†] Barrett, W.: Jour. Path. and Bact., vol. v, p. 345.

[‡] Rindfleisch: Lehrb. d. path. Gewebelch., S. 403.

[§] Nauwerck and Hufschmidt: Ziegler's Beiträge, Bd. xii, S. 1.

[||] Workman: Glasgow Hospital Reports, vol. ii, p. 363, 1900.

[**] Malassez: Progrès Médical, April 5, 1876.

[††] Claude: Bull. Soc. Anat. Paris, 1896, p. 117.

[‡‡] Sabourin: Archiv de Physiol., vol. xiv.

[§§] Pye Smith: Path. Trans., vol. xxxii, p. 112, 1881.

[||||] Pilliet: Tribune Médical, 1893.

This theory depends on the demonstration of the normal bile-ducts by the side of the cystic spaces. If this is not proved, and it has not appeared to me that it is thoroughly established, the spaces may still be regarded as dilated bile-ducts, for in any case the spaces and the bile-ducts arise from a common source—the duodenal diverticulum. The objections to the hypothesis that the spaces are dilated bile-ducts, viz., the absence of jaundice and the fact that injection driven into the larger bile-ducts does not enter the cysts, have been already considered.

Most writers accept Still's explanation, but personally I am not convinced that this view is more tenable than that cystic disease of the liver is due to some special form of fœtal cholangitis and pericholangitis.

CLINICAL PICTURE.

Cystic disease of the liver gives rise to no characteristic symptoms and is usually only found as a postmortem surprise. Its presence, however, may be suspected in a patient with greatly enlarged and probably cystic kidneys who has vague uræmic symptoms and considerable enlargement of the liver. In rare instances the cysts in the liver may be so large that they imitate hydatid or ovarian cysts. In Schroeder's case the abdomen was so widely occupied by the cystic liver that double multilocular ovarian cysts were diagnosed. A single large cyst may imitate a dilated gall-bladder. (Cleaver.) In practically all cases

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* Shattock, S. G.: Trans. Path. Soc., vol. xxxvii, p. 287.

† Still: Trans. Path. Soc., vol. xlix, p. 155.

‡ Cases quoted by Still, ibid., p. 164.

symptoms pointing to the liver are absent, and death, if not due to some intercurrent affection, is from uræmia. The cystic kidneys may be felt in life and sometimes have been regarded as hydronephroses, or even as pyonephroses.

A woman aged thirty-five was admitted into St. George's Hospital on October 8, 1902, with pain of one week's duration on the left side of the abdomen, where a soft, obscurely fluctuating tumor could be felt in the region of the kidney. There was pus in the urine, but no fever or leucocytosis. There had been dragging pain in the back from time to time and increased frequency of micturition, especially at night, for nine years. An exploratory operation by Mr. Allingham showed that both kidneys contained a large number of cysts of considerable size, and that the liver also contained a large number of cysts. A small piece of the liver containing some small cysts was removed. I examined it microscopically and found that the cyst walls were composed of well-formed fibrous tissue and that in the immediate neighbourhood the liver tissue showed fibrosis around the portal spaces. No epithelial or other lining could be found in the cysts.

Polydactylism and other external malformations are present in a majority of the cases seen in the newly born, but are not met with in adult cases. In the congenital case described by Kanthack and myself the infant, aged one month, was universally œdematous, had a large quantity of albumin in the urine, and was extremely drowsy, as if uræmic.

The **treatment,** if the condition be suspected, is that of chronic renal disease, the object being to prevent uræmia. Opening the cysts in the course of laparotomy has been done, but is useless, and should be avoided if the condition is recognised.

ADENOMA.

The subject of adenoma may be considered under the two heads of (I) single adenoma, (II) the so-called multiple adenomata which are nearly always found in association with advanced cirrhosis of the liver.

SINGLE ADENOMA.

An innocent encapsulated growth of epithelial cells may occur in the liver, but is decidedly rare; pathologically they are of great interest, but clinically they seldom attract attention.

True adenomata may theoretically be divided according to their structure into: (I) those composed of liver cells, or of cells derived from the ordinary cells of the hepatic parenchyma; (II) those derived from the bile-ducts; (III) those due to the inclusion of adrenal "rests."

I. Solitary Adenomata Derived from the Liver Cells.—An adenomatous tumor composed of liver cells, apart from the multiple growths of this kind seen in association with cirrhosis, is rare. Such growths may be spoken of as "acinous adenomata" in contradistinction to those derived from the bile-ducts, or as "solitary adenomata" in order to distinguish them from multiple adenomata.

Barbacci,[*] who has collected twelve examples of single adenomata, finds that they occur equally in the two sexes, and that the extremes of age are two and sixty-nine years.

Mahomed[†] described a localised collection of cells surrounded by a fibrous capsule embedded in the liver, which was "nutmeg"; the tumor did not share in this general change. I have seen one similar specimen. There is a specimen (2223*b*) of a single necrotic adenoma in St. Bartholomew's Hospital Museum. Hale White[‡] refers to an adenoma, 1¼ inches in diameter, projecting from the surface of the liver in the Guy's Hospital Museum. Specimens have also been described by Engelhardt[§] and others.

Possibly these tumors, which are pathological curiosities, may be due to some piece of liver substance which was separated during fœtal life from the main mass of the liver, becoming subsequently embedded in the organ. Not infrequently small projections of liver substance, miniature lobes, are seen on the under surface of the liver; if these became implanted in the substance of the liver, the appearance of an encapsulated adenoma, composed of liver cells, would be produced.

Cristiani[‖] refers to the existence of multiple nodules of hepatic tissue embedded under Glisson's capsule, which have been explained as congenital and due to the inclusion of tiny lobes. Pepere[**] supports the congenital origin of solitary adenoma

[*] Barbacci: La Clin. Mod., An. 6, No. 38, Sept. 19, 1900.
[†] Mahomed: Trans. Path. Soc., vol. xxviii, p. 144.
[‡] Hale White: Allbutt's System of Med., vol. iv, p. 210.
[§] Engelhardt: Deutsch. Archiv f. klin. Med., Bd. lx, S. 607.
[‖] Cristiani: Journ. de l'Anat. et Physiol., 1891, p. 271.
[**] Pepere: Archivio per le Scienze Mediche, vol. xxvi, p. 117, 1902.

and describes a case in which there were, in addition to one in the liver, innumerable minute encapsulated masses of liver tissue scattered over the peritoneum and omentum.

A simple adenoma is nearly always solitary; it is very rare that several are seen in the same liver. Multiple adenomata are nearly always accompanied by multilobular cirrhosis, and may be regarded as secondary to that condition and in the light of compensatory hyperplasias of the liver cells. A few examples of multiple adenoma without preëxisting cirrhosis are referred to on page 455.

In exceptional cases a solitary adenoma is found in a cirrhotic liver. Among twenty cases of solitary adenoma collected by Caminiti,* four were associated with cirrhosis (Jona,† Delaunay,‡ and two of his own). Possibly in some cases the association is a mere coincidence, Delaunay's case of a columnar-celled growth being probably of this nature. But in most cases it is probable that a "solitary adenoma" in a cirrhotic liver is only the initial stage of the multiple adenomata in cirrhosis. I have seen two cases bearing this interpretation.

Morbid Anatomy.—The tumor, often the size of a walnut, projects from the surface of the liver and is encapsuled. It is a yellowish or greenish white on section, and of the same consistence as normal liver, but does not share in any change, such as chronic venous engorgement, affecting the liver as a whole.

Microscopically the tumor is composed of liver cells which may, probably when the tumor is of some standing, be so modified as to form tubules lined by cubical epithelium, and in this respect resemble the structure of carcinoma with cirrhosis. The cubical character of the cells distinguishes this form of adenoma from the adenomata derived from the bile-ducts or from the mucous glands in their walls. In most cases the solitary adenoma derived from the liver cells is composed of cells of various sizes, but showing a general resemblance to the liver cells. There is no definite arrangement, but there are capillaries and some strands of fibrous tissue running through the tumor.

There are no clinical symptoms referable to this form of adenoma.

II. Adenomata Derived from the Bile-ducts.—A papilloma springing from the inside of the extra-hepatic bile-ducts would come under this heading, but is dealt with elsewhere. (*Vide* p. 681.) In this paragraph reference will be made to tumors arising from the intra-hepatic bile-ducts, indenting and displacing, but not invading, the surrounding liver substance; they may be described as tubular adenomata lined by columnar cells. It is possible that similar adenomata may be derived from the mucous glands in the walls of the larger bile-ducts. They may be single or multiple.

A *single adenoma* derived from the bile-ducts may become cystic; Leppmann§ has collected nine cases of this kind; under these conditions the adenoma may reach such a size that it may imitate malignant disease or hydatid cyst of the liver, or a floating kidney. The nature of such tumors can only be determined by laparotomy. Cases of this kind have been recorded by Keen, Shattuck, Schmidt.

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* Caminiti: Archiv f. klin. Chirurg., Bd. lxix, S. 630.

† Jona: Gazzetta d. Ospidali, 1901, No. 9.

‡ Delaunay: Bull. Soc. Anat. Paris, 1876, p. 241.

§ Leppmann: Deutsche Zeitschrift f. Chirurg., Bd. liv, S. 446, Feb., 1900.

Keen* removed a cystic adenoma, thought to be derived from the bile-ducts, from a woman aged thirty-one in 1891, who was alive in 1899. Clinically it was thought to be a floating kidney.

Shattuck's† case is well worth quoting: A woman aged sixty-three presented a tumor reaching from the right costal arch to the iliac crest. It was smooth, not tender, and presented a fluctuating area in the centre. At the laparotomy a cyst containing a gallon of clear fluid was found and drained. After some time bile came away from the sinus. A second operation was followed by death from cardiac failure. At the autopsy the cyst was found to arise from the liver near the falciform ligament and to have displaced the liver downwards. Microscopically the cyst wall showed numerous ducts and minute cysts, and it was regarded as a cystadenoma and not as a simple retention cyst.

It is quite possible that single adenomata of the bile-ducts of large size are sometimes regarded as cases of primary carcinoma of the liver.

Peugniez‡ operated upon a woman aged fifty-nine for a tumor diagnosed as a gall-bladder; an encapsuled tumor the size of the fist was removed and the patient recovered. The tumor was regarded as a primary massive carcinoma of the liver, but the description and figures given are quite compatible with the view that it was a large adenoma of the bile-ducts, like Keen's case.

Multiple adenomata derived from mucous membrane of the bile-ducts are occasionally met with (v. Hippel§). They may undergo cystic change, as in a remarkable case of Sigmund's‖ in a woman aged sixty-five. As has been pointed out (*vide* p. 450), multiple cystic disease of the liver has been regarded by Malassez, Claude, and others as a fibro-adenomatous growth of the bile-ducts.

III. Adenoma Due to Included Accessory Adrenal Bodies.—Schmorl** and Oberndorfer†† have shown that accessory adrenal bodies are sometimes found embedded in the substance of the liver. Schmorl found them in 4 out of 510 bodies. A case of an encapsuled tumor of the liver derived from an included suprarenal "rest" has been described by Schmorl, and it is probable that the development of simple adenomata in accessory suprarenal bodies implanted in the liver is not a very rare event, although only one has been described. Pepere‡‡ has described a primary malignant tumor of the liver arising in an accessory suprarenal body.

MULTIPLE ADENOMATA OF THE LIVER.

Synonyms: Nodular Hyperplasia; Nodular Hepatitis.

Multiple adenomata of the liver due to multiplication or hyperplasia of the liver cells are usually found in association with cirrhosis of the liver.

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* Keen, W. W.: Boston Medical and Surgical Jour., 1902, vol. i, p. 804. Annals of Surgery, 1899, p. 267.

† Shattuck: Boston Medical and Surgical Journ., April 26, 1900, p. 427.

‡ Peugniez: Bull. Soc. Anat. Paris, 1902, p. 456.

§ v. Hippel: Virchow's Archiv, Bd. cxxiii, S. 473.

‖ Sigmund: Virchow's Archiv, Bd. cxv, S. 155.

** Schmorl: Ziegler's Beiträge, Bd. ix, S. 523, 1891.

†† Oberndorfer: Centralblatt f. allg. Path. u. path. Anat., Bd. xi, S. 145, 1900.

‡‡ Pepere: Archiv. de Méd. Expérimental et d'Anat. path., 1902, p. 765.

This is probably because cirrhosis is the commonest disease which destroys the liver cells and renders a compensatory hyperplasia necessary; but considerable discussion has taken place as to the relationship between cirrhosis and adenomata. Nodular hyperplasia may be met with in the absence of cirrhosis, as in some cases of malarial infection, occasionally in cases of acute yellow atrophy which run a protracted course, and in rare cases of chronic venous engorgement of the liver. The terms "nodular cirrhosis" and "cirrhosis complicated with adenoma," though descriptive of the vast majority of multiple adenomata, from hyperplasia of the liver cells, cannot be used as synonyms for multiple adenomata.

J. Bartels[*] draws a distinction between multiple adenomata which are surrounded by a fibrous capsule, and nodular hyperplasia where there is no capsule.

Relationship of Multiple Adenomata and Cirrhosis.—Kelsch and Kiener,[†] and more recently Dieulafoy and Engelhardt,[‡] believe that the cirrhosis and the adenomata are due to the same poison and are the concomitant results of proliferation of the framework and of the cells of the liver respectively. Dieulafoy[§] regards the two processes as not only independent, but simultaneous. In support of this it may be urged that in dogs tumors due to hyperplasia of the liver cells, and probably set up by infection, are far from rare; here the irritation attacks the epithelial instead of the fibrous parts of the organ. A condition allied to this is seen in the Fuegians as the result of eating mussels, which at certain periods of the year contain a chemical poison; the liver shows enlargement due to hyperplasia of the liver cells and subsequently becomes cirrhotic. (Segers.[‖]) As the result of injection of the blastomycetes, regarded as the parasite of cancer by San Felice, Wlaeff[**] produced adenomatous tumors in the livers of guinea-pigs. Areas of circumscribed hyperplasia of the liver cells are described in the liver in some cases of malaria and have been seen in a nutmeg liver. (Jacobi,[††] Earl.[‡‡])

A man aged thirty-seven died in St. George's Hospital in February, 1903, with advanced pulmonary tuberculosis and tuberculous peritonitis. The liver was at first thought to be stuffed with caseous tubercles. Microscopically these white areas were found to be multiple adenomata; the liver showed no cirrhosis.

Cornil and Ranvier[§§] and Schmieden[‖‖] regarded the adenomata as a complication of and secondary to cirrhosis of the liver. Brissaud[***] described multiple adenomata as a half-way house between cirrhosis and primary carcinoma, and the term "hepatoma" was suggested by

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[*] Wien. klin. Wochen., 1904, S. 613.

[†] Kelsch and Kiener: Archiv de Physiol., 1876, p. 622.

[‡] Engelhardt: Deutsches Archiv f. klin. Med., Bd. lx, 1898.

[§] Dieulafoy: Manuel de path. Intern., tome ii, 734, 1901.

[‖] Segers: La Sem. Méd., p. 448, 1891.

[**] Wlaeff: Journ. de Méd., Paris, Jan. 20, 1901, p. 27.

[††] Jacobi, A.: Trans. Assoc. American Physicians, vol. xii, p. 493.

[‡‡] Earl: Lancet, 1902, vol. ii, p. 1464.

[§§] Cornil et Ranvier: Manuel d'histologie pathologique, tome ii, p. 438.

[‖‖] Schmieden: Virchow's Archiv, Bd. clix, S. 290.

[***] Brissaud: Archiv. Général. de Méd. 1885, tome ii.

Sabourin[*] to describe the transitional stage between adenoma and carcinoma. Lancereaux[†] took the extreme view that cirrhosis was due to irritation set up by the presence of the adenomata.

There is some confusion in literature between cirrhosis with multiple adenomata and primary carcinoma with cirrhosis. It appears that Sabourin, who uses the former term, is sometimes describing cases which Hanot and Gilbert would call primary carcinoma with cirrhosis. The innocent condition of multiple adenoma in cirrhosis may eventually pass into primary carcinoma. When this occurs, there will be evidence of the growth infiltrating the walls of the portal or hepatic veins or of secondary growths in the lungs or elsewhere.

Nature of Multiple Adenomata.—These multiple adenomata are nearly always, at any rate in England, associated with cirrhosis. Some reservation is necessary, since nodular hyperplasia or multiple adenomatous formations are found in cases of chronic malarial infection, and exceptionally under other conditions already mentioned. The multiple adenomata ordinarily met with are exaggerations of the hobnails seen in portal cirrhosis, and represent a further stage of nodular hyperplasia. Multiplication of the more healthy liver cells occurs in common or portal cirrhosis and contributes to the size of the hobnails and to the increased weight of the liver in latent cirrhosis. It is when these hobnails undergo fatty degeneration and necrosis, and appear white on section, that they are particularly liable to attract attention, for when this change has occurred they do not, unless bile-stained, suggest cirrhosis, but resemble multiple new-growths or even caseous tubercles. Fatty change and necrosis of the hyperplastic nodules are particularly likely to occur when thrombosis of the portal vein is superadded to cirrhosis; hence the frequency with which portal thrombosis is recorded as associated with multiple adenoma, cancer with cirrhosis, etc. Thus in 15 cases of so-called adenoma of the liver that were analysed by Dr. L. Powell,[‡] no less than 9 had thrombosis of the portal vein.

Those who regard the condition as one of primary carcinoma of the liver adduce the presence of hepatic cells in the portal vein and thrombosis as further proof of its malignant character. But the presence of some hepatic cells in the portal vein does not absolutely prove that the growth is malignant, for the hobnails, being poorly nourished and having by rapid proliferation outgrown their blood-supply, soften down and may discharge into the portal vein or hepatic veins, and so induce thrombosis. Microscopic examination of the thrombus shows badly formed blood-clot with débris and large fatty liver cells.

Delépine[§] drew attention to this discharge of softened adenomata into the portal and hepatic veins, and F. C. Turner[‖] described liver cells and fragments of liver tissue in the portal veins of cirrhotic livers and suggested that it was due to damage of the vessel walls by the septic process which was present in both his cases.

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[*] Sabourin: Thèse Paris, 1881. Rev. de Méd., 1884, p. 321.

[†] Lancereaux: Gaz. Médicale, 1868.

[‡] Unpublished Thesis for M. B. degree, Cambridge, 1895.

[§] Delépine, S.: Trans. Path. Soc., vol. xli, p. 363.

[‖] Turner, F. C.: Ibid., xxxv, p. 22; and vol. xxxvii, p. 262.

The proliferation of the liver cells may be due to one of two causes, and very possibly to each of the causes at different stages of the disease:

(I) The multiplication of the hepatic cells in the hobnails may be set up by the same poison that stirs up the connective tissue of the liver to proliferation; this would be the case especially in the early stages of the disease. In cases of poisoning by mussels similar nodules are produced, evidently directly due to the irritation exerted by the poison.

(II) The multiplication of the liver cells may be an attempt at compensation to make good the functional activity of the liver as a whole, which has been greatly reduced by the destruction of hepatic tissue.

In favour of the view that the change is compensatory are the facts: (*a*) that the adenomatous formations are found in portal cirrhosis, where degeneration and destruction of the liver cells are marked features, and (*b*) that they are absent in hypertrophic biliary cirrhosis, where the liver cells retain their vitality for a long time.

Compensatory hyperplasia of the liver cells occurs in the most diverse conditions, which all have only one factor in common, viz., interference with the functional activity or destruction of the liver cells. The effects of removal of portions of the liver in animals have been investigated by Tizzoni, Ponfick,* v. Meister, Floeck, Zadoc-Kahn,† and others. Proliferation begins and is most active, probably because nutrition is best there, in the liver cells at the periphery of the lobules. The compensatory hyperplasia in cirrhosis is of two kinds: (i) the earlier gives rise to the formation of the so-called new bile-ducts; (ii) the other, which occurs later, is that seen in the so-called adenomata.

When multiple adenomata in cirrhosis are seen at the autopsy of fatal cases of cirrhosis, the compensatory mechanism has in most cases broken down, and is often explained by thrombosis of the portal vein The compensation may also be nullified by degenerative processes, fatty change or softening in the hyperplastic hobnails, or by fibrosis spreading into them. No doubt the large size of livers in latent cirrhosis is partly due to this compensatory hyperplasia of the liver cells. (See also Prognosis of Portal Cirrhosis.) Nodular cirrhosis is not very infrequently seen in cases fatal from pulmonary tuberculosis, and may be looked upon as a compensated cirrhosis. In such cases, if fatty degeneration attacks the hobnails, an appearance suggesting caseation results; it is quite possible that a naked-eye examination of the liver might result in a diagnosis of extensive tubercle or new-growth of the organ.

Morbid Anatomy.—The appearance of the liver is very striking and suggests multiple secondary new-growths, gummata, or even caseous tubercle. The surface of the liver shows numerous projecting nodules, which, however, are not umbilicated. They are white on section, usually dry and friable, but may, especially when associated with portal thrombosis, be softened. The surrounding liver substance may be deeply congested, so that the contrast between the hobnails and the rest of the liver still further suggests secondary malignant disease. Adenomata in children with cirrhosis may be extremely prominent, and to the naked eye very closely resemble malignant disease; probably this active proliferation is part of a child's inherent power of repair and growth. The liver is usually enlarged, and sometimes to a very great extent. It is only rarely that it is actually smaller than natural.

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* Ponfick: Virchow's Archiv, Bd. cxviii, cxix.

† Zadoc-Kahn: Archiv. Général. de Méd., 1897, p. 165.

It is impossible to draw a hard-and-fast line between a markedly hobnailed liver, nodular cirrhosis, and cirrhosis with multiple adenomata; the conditions pass into each other, and what one observer might speak of as extreme cirrhosis might by another be called cirrhosis with adenoma. The portal vein is frequently thrombosed, and microscopic examination of the clot may show a few liver cells due to the discharge of one of the softened hobnails into the vein. Sometimes similar thrombosis is seen in the hepatic veins. The lymphatic glands in the portal fissure are not enlarged.

Microscopically the liver shows marked cirrhosis; the masses which to the naked eye suggest new-growth are altered liver cells surrounded by a fibrous capsule; the interstitial tissue shows the appearance of pseudo-bile canaliculi, advancing cirrhosis, and sometimes extravasated blood. In a hyperplastic nodule examined at an early stage the liver cells are larger than natural, in a good state of nutrition, and, as shown by karyokinetic figures, are undergoing active proliferation. This stage may be spoken of as nodular cirrhosis. In an early stage the naked-eye appearances are more striking than the microscopic. The first impression on looking at a microscopic section of nodular cirrhosis is often one of disappointment at finding little more than the changes of cirrhosis. As growth proceeds the cells in the centre of the nodule become the bigger, while those at the periphery become flattened from pressure and may become spindle-shaped. The normal arrangement of the hepatic lobule is lost, and tortuous columns of cells are seen which often tend to form irregular circles around the intralobular vein. The cells forming this anastomosing network are cubical and are larger than those forming the so-called new bile-ducts, but are usually smaller than the liver cells. At this later stage the adenoma has become tubular. Multinuclear large cells are occasionally present in the centre of the adenomatous nodule, and, according to Schmieden, proliferate to form the adenomatous cells. Hæmorrhage may occur into the adenomata or around them, and fatty change may appear in the cells forming the adenomata, especially when the portal vein is thrombosed. Fibrosis may extend into the substance of the adenomata.

Secondary Changes in Multiple Adenomata.—The fatty metamorphosis of the cells already mentioned may lead to softening down of the adenomata and the formation of the cystic spaces. The adenomata may discharge into the branches of the portal or hepatic veins and set up thrombosis. From vigourous proliferation of the cells in the adenoma the process may become carcinomatous; this condition is fully described in the section on "Carcinoma with Cirrhosis."

Clinical Aspect.—Since multiple adenoma is usually a result of cirrhosis, its age and sex incidence, its signs and symptoms, treatment, etc., are much the same as in that disease. It is found in a high proportion of those cases where at the autopsy cirrhosis with thrombosis of the portal vein is present, and is therefore very frequently associated with ascites and hæmatemesis. An attempt has sometimes been made to establish a difference between the clinical features of ordinary cirrhosis and multiple adenomata, and the tendency has been rather to lay stress on the presence of hepatic pain and to present a picture approaching that of malignant disease of the liver. But no reliance can be placed on any such clinical differences.

ANGIOMA.

Synonyms: Cavernoma; Nævus.

The liver is more often the seat of angiomata than any viscus in the body, but angiomata are not very common in the liver; Lancereaux[*] has seen 25 cases. They are more frequently seen in the livers of cats. As to the incidence of the ordinary acquired nævi in the two sexes, Hanot and Gilbert[†] say they are commoner in men, while Thoma[‡] states that they are more frequent in women. They may be congenital and have been seen in fœtuses, though this is somewhat exceptional; they are then probably due to some disturbance in the process of development. Usually, however, they are found in the bodies of persons advanced in years and are then more probably acquired and may be due to a combination of local congestion of the hepatic vessels and atrophy of the liver cells. Usually they are quite small. When they form large tumors, the patients are, as a rule, very young, though very occasionally large cavernous tumors have been seen in adults.

In Fillipini's[§] case there was a tumor as large as an adult's head in the left lobe of the liver in a woman aged twenty-two. In Mantle's case[‖] the tumor which had been growing for two years, in a man aged thirty-three years, was thought to contain 8 pints of blood.

They may be multiple, but are more often single. As many as 30 have been seen in the same liver. In Schmieden's[**] 32 cases, 18 were single, 14 multiple. Angiomata may be found at the same time in other abdominal viscera.

In Payne's[††] case there were exceptionally large cavernous angiomata in the liver, which weighed 6 pounds, and angiomata in both ovaries and both adrenal bodies; while in Petroff's[‡‡] case there were angiomata in both adrenal bodies.

Morbid Anatomy.—Their most common situation is immediately under the capsule, and often near the edge of the liver, on the convexity or in the neighbourhood of the falciform ligament. After death they become partially empty and are therefore slightly depressed below the level of the surrounding liver substance. In exceptional cases they become pedunculated. Lancereaux[§§] figures a pedunculated angioma attached to a liver which also contained other angioma; and Journiac* has also described this condition. They are round or wedge-shaped, with the base directed outwards and the apex inwards so as to resemble closely that somewhat rare lesion, a hæmorrhagic infarct in the liver. On section they have a honeycombed appearance when the blood has been removed, like that of erectile tissue of the corpus cavernosum penis or of the placenta. They are dark red in colour; occasionally the surrounding liver substance is darkened by infiltration with black pigment derived from the blood. They are sometimes encapsuled or encysted, and in connexion with this it is interesting to note that Berard Aîne † suggested they were encysted splenic "rests." When the cavernous tumors are large there is usually a fibrous capsule, while in smaller specimens there is often none, and the cavernous tissue is in immediate contact with the liver cells. It is possible that the encapsulation is a secondary process and develops around old nævi, as in the case of other innocent tumors. In a case recorded by Cripps ‡ the capsule showed calcification. Considerable difference of opinion has been expressed as to their connexions with the other vessels in the liver, and they have been said to be only connected with the veins or to be in free communication both with the hepatic artery and with the portal and hepatic veins. There does not seem to be any tendency to malignant (endotheliomatous) change in them.

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[*] Lancereaux: Traité des Maladies du foie et du pancreas, p. 528.

[†] Hanot and Gilbert: Études des Maladies du foie, p. 315.

[‡] Thoma: Pathology, English Trans. by Bruce, vol. i, p. 553.

[§] Fillipini: Il Policlinico, April, 1901. *Vide* Epitome, Brit. Med. Journal, 1901, ii, No. 94.

[‖] Referred to Brit. Med. Journ., 1902, vol. ii, p. 423, and described in the same journal, 1903, vol. i, p. 365.

[**] Schmieden: Virchow's Archiv, Bd. clxi, S. 373.

[††] Payne, J. F.: Trans. Path. Soc., vol. xx, p. 203.

[‡‡] Petroff: Bolnichnaya Gazeta Botkina, 1899, No. 30; abstract in Rev. de Méd., 1901, p. 920.

[§§] Lancereaux: Traité des Maladies du foie et du pancreas, p. 528, 1899.

Besides the pigmented or "melanotic" and the encysted angiomata, there is another variety described—the fibrous angioma—in which the trabeculæ increase markedly in thickness and thus tend to lead to obliteration of the cavities or to its cure. It is possible that by degenerative changes these nævi may become transformed into serous cysts.

Histologically there is a communicating meshwork of spaces containing red blood-corpuscles. The walls of the spaces are composed of fibrous tissue with a certain number of young connective-tissue cells and some elastic fibres. Smooth muscle fibres are described in some specimens. The spaces are lined by flattened endothelial cells covering the surface of the fibrous trabeculæ. The structure is therefore that of cavernous tissue. I have seen a specimen entirely composed of vessels and quite devoid of blood sinuses. The tumor may be separated from the liver cells by a layer of fibrous tissue which serial sections show to be continuous with Glisson's capsule. In many specimens there is no limiting capsule and the blood-spaces are in direct contact with the liver cells, which may form columns running into the cavernous tissue. Bile-ducts and liver cells may thus appear to be embedded in the tumor. Pigment granules may be found in the fibrous trabeculæ as well as in the surrounding liver cells; Hanot and Gilbert § give an illustration of this under the title of "melanotic angioma."

Secondary Changes.—The blood may clot in the cavernous spaces and the endothelium may then creep over the remains of the clotted blood. When the blood-supply is interrupted by thrombosis, the cavernous tissue may become modified so as to contain serous fluid and imitate a lymphangioma. In other cases the fibrous framework of the tumor may proliferate and compress and eventually obliterate the blood-spaces; in other instances hyaline degeneration may occur in the fibrous stroma.

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* Journiac: Archiv de Physiol. norm. et path., 1878, p. 37.

† Berard Aîne: Bull. Soc. Anat. Paris, 1828, p. 9.

‡ Cripps, W. Harrison: Brit. Med. Journ., 1903, vol. ii, p. 18.

§ Hanot and Gilbert: Études des Maladies du foie, p. 341.

Pathogeny.—Different views have been put forward to explain the formation of angiomata in the liver, and it is probable that all angiomata are not due to the same process. The congenital ones may with a fair show of reason be referred to a different pathological process from that responsible for those observed late in life (acquired angiomata). The following views may be mentioned:

(I) That they are a malformation due to an excessive growth of the vascular mesoblast. This would account for the congenital angiomata, which in rare instances reach a sufficiently large size to be clinically recognisable as tumors. Schmieden,* who does not believe that hepatic angiomata are the same as those met with elsewhere in the body, for example, the cutaneous angiomata, refers their formation to a malformation or congenital defect and suggests the new term "cavernoma," or "nævus cavernosus hepatis."

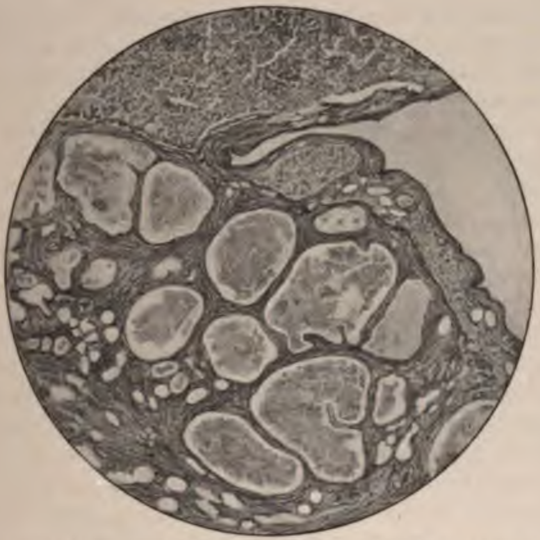

FIG. 57.—DRAWING OF ANGIOMA (CAVERNOMA) OF THE LIVER, SHOWING SPACES CONTAINING COAGULATED BLOOD WITH FIBROUS ALVEOLAR WALLS. IT IS ENCAPSULED. × 21.

(II) That there is a development of new blood-vessels in connexion with a new formation of fibrous tissue, the vessels being derived from preëxisting ones in the neighbourhood. In other words, there is an innocent angiofibroma. This explanation of Virchow's[*] does not account for angiomata devoid of a fibrous tissue capsule. Again, if this were the true explanation, it would be natural to expect to find angiomata frequently in cirrhosis. Though new vessels, sometimes in considerable numbers, are seen in the newly formed fibrous tissue, definite angiomata are rare.

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* Schmieden: Virchow's Archiv, Bd. clxi, S. 373.

(III) The view of Cornil and Journiac is a modification of the preceding, and is to the effect that there is in the first instance an embryonic proliferation of the perivascular tissue of preëxisting veins and capillaries, which brings about dilatation of the vessels, and that eventually these vessels communicate.

(IV) That stagnation of blood and congestion induce dilatation of the vessels with atrophy of the intervening liver cells. Some increased fibrosis takes place, so that a cavernous nævus is produced. This theory, supported by Chervensky,[†] and by Hanot and Gilbert,[‡] explains satisfactorily the acquired angiomata, and especially those which fade off into the liver tissue without any intervening fibrous capsule. The formation of fibrous tissue around a hepatic angioma may very probably be a secondary process, and the same as the encapsulation of other innocent tumors, hence the presence of a fibrous capsule is not necessarily a strong argument against the method of formation. Though typical angiomata are not commoner in the livers of chronic venous engorgement than in other conditions, microscopically areas showing angiomatous capillaries are of course common in nutmeggy livers. On the other hand, this method does not explain congenital angiomata or those in early life.

Primary atrophy of the liver cells alone will not account for the formation of angiomata, since it is not an infrequent event and is not accompanied by angiomata. As already pointed out, it is unnecessary to refer all hepatic angiomata to the same method of origin. Some are due to congenital maldevelopment, while others are due to vascular engorgement combined with atrophy of the liver tissue.

Clinical Aspect.—There is no relation between the amount of interest that attaches to the pathology of angiomata of the liver and their clinical bearing. In the vast majority of cases no symptoms can be put down to the presence of angiomata in the liver. It has been suggested that murmurs or venous hums heard over the hepatic region are sometimes produced in this way. In exceptional examples they have reached a considerable size; thus Stiffen,[§] Chervensky,[‖] Mantle, Cripps, and others have met with considerable hepatic enlargement from this cause.

In Petroff's[**] case of a woman aged thirty-eight years with symptoms of Addison's disease jaundice was found to be due to the pressure exerted by a large angioma of the liver on the bile-ducts. There were cavernous angiomata in both the suprarenal bodies. A fibrinous nævus compressed the right hepatic and the cystic ducts and gave rise to jaundice, colic, and distension of the gall-bladder. It was successfully removed by Tédenat.[*]

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[*] Virchow: Virchow's Archives, Bd. v, S. 525.

[†] Chervensky: Archiv de Physiol., 1885, t. ii, p. 553.

[‡] Hanot and Gilbert: Études sur les Maladies du foie, p. 316, 1888.

[§] Stiffen: Jahrb. f. Kinderheilk., 1883, S. 348.

[‖] Chervensky: Archiv de Phys., 1885, ii, 552.

[**] Petroff: Bolnichnaya Gazeta Botkina, 1899, No. 30. Abstract in Rev. de Méd., 1901, p. 920.

In some cases the condition has been diagnosed as hydatid or merely as a doubtful tumor of the liver.

I am indebted to Dr. Seymour Taylor for the notes of a case where a man had a tumor in connexion with the liver which closely imitated a hydatid cyst; it was operated upon, and when exposed, still resembled a cyst; on puncture it bled profusely at every point and the hæmorrhage was with difficulty arrested. The patient left the hospital well.

The prognosis is fairly good in the cases which are operated upon, which as a matter of fact are the only ones which can be diagnosed with certainty during life.

Treatment.—As it is only exceptionally that hepatic angiomata give rise to any signs or symptoms, the question of treatment rarely arises. As the presence of a large angioma would imitate a tumor of the liver, the only method of treatment is surgical, but there is considerable danger of profuse hæmorrhage. If the tumor was thought to be an angioma, electrolysis might be tried. Keen,[†] in a list of 75 cases where resection of the liver has been done for neoplasms, refers to 4 cases of angioma thus treated. A large nævoid growth, at first regarded as an ossifying sarcoma, was recently successfully removed from the liver by Cripps.[‡] In 1904 Tédenat could only refer to six cases in which excision had been carried out.

LYMPHANGIOMA.

It is possible that a tumor of this nature may occur in the liver occasionally, but I have only been able to find a description of one case, Maresch's,[§] in which a pedunculated tumor, diagnosed as an ovarian cyst, was removed from the right lobe of the liver of a girl aged five years. It is quite conceivable that a tumor of this kind might result from degenerative changes in an angioma of the liver.

MYXOMA.

A very large growth in the liver of a patient who had previously had a tumor removed from the breast by Mr. Nunn[‖] was described by the Morbid Growths Committee of the Pathological Society as a myxoma. Though probably a myxo-sarcoma, this specimen has often been referred to as a myxoma of the liver. A few other cases of myxoma have been described, but it seems probable that they are allied to sarcomatous rather than to innocent tumors. Cornil and Cazalis[**] described a primary myxoma in the liver of a child of nine months.

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[*] Archiv. gén. de Méd., Mar. 8, 1904, p. 586.

[†] Keen: Annals of Surgery, Sept., 1899, p. 276.

[‡] Cripps: Brit. Med. Journ., 1903, vol. ii, p. 18.

[§] Maresch, R.: Zeitschrift f. Heilkunde, Bd. xxiv, S. 39, 1903

[‖] Nunn, T. W.: Trans. Path. Soc., vol. xxiv, p. 120.

[**] Cornil and Cazalis: Gaz. Méd. de Paris, 1872, p. 539

FIBROMA.

A few examples of fibromata of the liver have been described, but some caution must be exercised in accepting their existence. When this condition is met with in infants it may be a manifestation of congenital syphilis and belongs to the group of cases described by Marchand.* Luschka's † case of fibroma in a child one month old was probably of this nature. It is possible that other cases would be more correctly described as fibro-sarcomata; while it is conceivable that an angioma might undergo fibrotic atrophy and eventually form a small fibrous tumor.

Lancereaux‡ described a fibroma infiltrated with calcareous salts, in a woman aged twenty-eight years. On the under surface of the right lobe of the liver of a woman aged fifty-six Chiari § found a fibroma the size of an egg. Four calcified fibromata, varying in size from a nut to a grain of wheat, were found in the liver of a tuberculous woman. (Pisenti. ‖) In a case of multiple neurofibromata the sympathetic nerves in the liver were beset with fibromata from the size of a bean to that of a millet seed. (Ziegler.**)

LIPOMATA.

Genuine fatty tumors are not met with in the liver. But what might be spoken of as a lipoma may be found indented on the surface but outside the capsule of the liver: these small tumors are in reality appendices epiploicæ which have become detached from the colon and have come to rest between the diaphragm and the convexity of the liver.†† I have now seen several examples of this condition. An encapsulated mass of fat of about the size of a nut is found in a depression on the convexity of the liver, which it tightly fits. The capsule of the liver passes between the fatty body and the liver substance and there is no vascular connexion between the fatty tumor and the liver.

Localised areas of extreme fatty change in the liver cells are sometimes met with; they probably depend on vascular obstruction and microbic activity, and are not likely to be mistaken for real fatty tumors. The fat which accompanies the obliterated umbilical vein in the falciform ligament sometimes increases in size so as to resemble a small fatty tumor. I have seen an example of this in a woman who died from the effects of herniotomy.

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* Marchand: Centralblatt f. allg. Path., Bd. vii, S. 273, 1896.

† Luschka: Virchow's Archives, Bd. xv, S. 168.

‡ Lancereaux: Atlas d'Anat. path., 1871.

§ Chiari: Wien. med. Wochens., 1877, S. 365.

‖ Pisenti: Quoted by Pepere, I Tumori maligni primarii del Fegato, p. 25, 1902.

** Ziegler: Special Pathological Anatomy. Translated by Macalister, Part ii, p. 342, 1884.

†† Rolleston: Trans. Path. Soc., vol. xlii, p. 160.

EMBRYOMATA AND TERATOMATA.

These are extremely rare in the liver, and are merely pathological curiosities.

Hanot and Gilbert* refer to a single instance of a cyst in the liver containing hair, cartilage, and fatty material. In a baby aged six weeks Misick† found a lobular tumor the size of a man's fist in the right lobe of the liver; it contained bone, cartilage, and cysts derived from the hypoblast, but no epiblastic elements, so it should be described as a teratoma rather than a dermoid cyst. During life it was thought to be a tumor of the right kidney.

Pye Smith‡ described a case of a teratoma adherent to but not arising from the liver in an infant one year old. During life the tumor had been tapped several times and the disease was regarded as multilocular cystic disease of the liver. It was an included fœtus.

The secondary implantation on the surface of the liver of fragments of a ruptured ovarian embryoma is referred to on page 501. A case of this kind was described by Hulke.§

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* Hanot and Gilbert: Études sur les Maladies du foie, p. 295, 1888.

† Misick: Jour. Path. and Bacteriol., vol. v, p. 128.

‡ Pye Smith: Trans. Path. Soc., vol. xxxvii, p. 499.

§ Hulke: Trans. Path. Soc., vol. xxiv, p. 157.

MALIGNANT DISEASE OF THE LIVER.

The subject of malignant disease of the liver will be considered in the following way: First the incidence and a detailed account of the morbid anatomy of primary malignant disease; then the incidence and a detailed description of the morbid anatomy of secondary malignant disease; thirdly, the general clinical picture; and, lastly, the points of distinction between the clinical manifestations of primary and secondary malignant disease of the liver.

PRIMARY MALIGNANT DISEASES OF THE LIVER.

INCIDENCES.

Primary malignant disease of the liver is a rare disease. Every case requires critical portmortem investigation to make sure that it is not secondary to some obscure growth elsewhere, and that the growth did not, in reality, start in the gall-bladder or larger bile-ducts.

In 11,500 autopsies at Guy's Hospital, Hale White[*] found 11 cases of primary carcinoma of the liver, or 0.1 per cent. Eggel[†] estimates that primary carcinoma occurs once in 2000 autopsies, or 0.5 per cent.

The numerical ratio between primary and secondary carcinoma of the liver has been placed between 1:20 and 1:40. (*Vide* p. 485.)

Primary sarcoma, in which endothelioma is also included, of the liver is rarer even than carcinoma.

Leith[‡] collected 25 cases in 1897. In 1901 Vecchi and Guerrini[§] critically examined 45 published cases of primary sarcoma of the liver, but only accepted 21 cases as undoubted examples of this rare condition. I have notes of 64 cases of reputed primary sarcoma, of which 32 occurred in patients over ten years of age and 32 under that age. These cases do not include those described as primary melanotic sarcoma (*vide* p. 483) or any which appeared to be most probably cases of hepatitis due to congenital syphilis.

Sex.—Primary malignant disease of the liver seems to be more frequent in men than in women, and contrasts with primary carcinoma of the gall-bladder, which, like gall-stones, is infinitely commoner in women—gall-stones and carcinoma of the gall-bladder being both about four times more frequent in women than in men.

In 74 cases of primary malignant disease in adults (42 carcinoma, 32 sarcoma) which I have collected, 42 were males and 32 females. The male sex was more often affected by carcinoma; of the 42 cases, 29 being males and 13 females. In Eggel's collection of 163 cases of primary carcinoma 63 per cent. were males. Among the 32 cases of primary sarcoma 19 were females and 13 males.

Age.—Primary carcinoma of the liver occurs in or after middle life and is rare before forty years of age.

In 42 cases of primary carcinoma (males 29, females 13) the average age was 47.2 years, being 42.1 among the females and 49.3 among the males.

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[*] Hale White: Allbutt's System of Medicine, vol. iv, p. 197.

[†] Eggel: Ziegler's Beiträge, Bd. xxx, S. 506, 1901.

[‡] Leith: Lancet, 1897, vol. i, p. 170.

[§] Vecchi and Guerrini: Medical News (New York), Nov. 23, 1901, p. 816.

The earlier observers described cases of cancer or "scirrhus" in very young children, but most of them were probably sarcomatous or due to congenital syphilis.

Comparatively recently Prescott* recorded a congenital carcinoma of the left lobe of the liver in an infant of five months, but it is highly probable that it was an endothelioma.

In older children portal cirrhosis with multiple adenoma very closely resembles carcinoma. H. Fussell and Kelly's† case of primary carcinoma in a girl aged sixteen years was regarded by Welch and Dock in this light.

Dr. Still has given me sections of a child's liver which looked exactly like malignant disease to the naked eye, but microscopically showed cirrhosis with compensatory hyperplasia of the liver cells.

Acland and Dudgeon‡ described an undoubted case of primary carcinoma of the liver in a boy aged fifteen years, in which the liver weighed nearly 16 pounds, and collected eight other cases of primary carcinoma of the liver under twenty years of age.

Acland and Dudgeon's cases are those of Ollivier, Deschamps, Kottman, Henschen, Pye Smith, Birch-Hirschfeld, and Fussell and Kelly. There is considerable doubt as to Ollivier's, Fussell and Kelly's, and one of Birch-Hirschfeld's cases being genuine carcinoma. An interesting case of primary carcinoma in a woman aged twenty-two years has been recorded by Gilbert and Claude.§

Primary sarcoma may occur at almost any age. The oldest case of which I have a reference was seventy-three years, while congenital cases have been recorded. Primary sarcoma of the liver may, like sarcoma of the kidney, be divided into two categories: (*a*) those which occur in adult life and (*b*) those met with very early in life.

The average age of 32 cases occurring in patients over fifteen years of age was 47.53 years (males, 51.6 years; females, 44.7 years), or exactly the same as the average age for primary carcinoma of the liver. In addition to these 32 cases I have tabulated 32 cases of primary sarcoma of the liver under ten years of age.

In 1883 Picot ‖ made a collection of 424 cases of malignant disease occurring under seventeen years of age, which included 13 of primary malignant disease of the liver. R. Williams** referred to 29 cases of primary malignant disease of the liver under the age of fifteen years, the majority of which were probably sarcomatous. Nœgerrath†† described a case of primary malignant disease of the liver in a baby which interfered with delivery; a congenital case was also observed by Jacobi.‡‡

In connexion with sarcoma occurring in early life a caution must be thrown out as to the danger of regarding as sarcoma the lesions of congenital syphilis. Cases of pericellular cirrhosis in infants have been

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[*] Prescott: Boston City Hospital Reports, 1895.

[†] Howard Fussell and Kelly: University Med. Magazine, Aug., 1895.

[‡] Acland and Dudgeon: Lancet, 1902, vol. ii, p. 1310.

[§] Gilbert and Claude: Arch. général. de Méd., t. clxxv, 1895, p. 513.

[‖] Picot: Rev. Med. de la Suisse Romande, 1883, p. 660.

[**] R. Williams: Lancet, 1897, vol. i, p. 1328.

[††] Nœgerrath: Deutsche Klinik, Bd. vi, S. 496, 1894.

[‡‡] Jacobi: Therapeutics of Infancy and Childhood, p. 371.

described as primary sarcoma, lymphosarcoma, etc. A diffuse pericellular cirrhosis in fœtal life is, like sarcoma, an embryonic connective-tissue growth, so that the two processes have much in common. Severe visceral syphilis in early life may, as shown by Morley Fletcher's * case, give rise to hæmorrhagic enlargement of the suprarenal bodies. Such a case might easily be regarded as sarcoma of the liver with secondary growths. Secondary growths in the adrenals may occur in primary sarcoma of the liver (Guy's Museum, No. 1571), or growths may be found in both organs and it may not be easy to say which of the two is the primary growth.

Pepper † has collected six cases of congenital sarcoma of the liver and adrenal glands; the question of syphilis as the real change is fully considered by him, but not admitted.

ETIOLOGY.

This is not the place to discuss the large and unsettled problem as to the true cause of malignant disease or to consider the "parasitic" or "habit of growth" theories on the question. There is, however, one form of primary carcinoma in the liver, viz., that which develops in a previously cirrhotic liver, which favours the view that carcinoma is due to the acquired habit of proliferation of the liver cells, which, starting as a compensatory hyperplasia and thus giving rise to multiple adenoma in cirrhosis, eventually becomes so excessive as to constitute carcinoma.

In a few cases a definite history of a blow on the abdomen preceding the onset of malignant disease is forthcoming and may possibly have played some part in starting cellular proliferation.

MORBID ANATOMY.

Situation of the Growth in Primary Malignant Disease of the Liver.—Primary malignant disease of the liver usually arises in the right lobe, but occasionally is limited to the left lobe.

As a curiosity, reference may be made to malignant disease arising in a tongue-like lobe. In a case of calculous cholecystitis and pericholecystitis the pendulous lobe in connexion with the gall-bladder was found to be the site of primary carcinoma; at first sight it was thought to have started in the gall-bladder, but Roux ‡ satisfied himself that this was not the case.

On the other hand, the growth may infiltrate both lobes, so that it is impossible to make out where it started, or there may be multiple primary growths in both lobes.

The morbid anatomy will be considered under the two heads of Primary Carcinoma and Primary Sarcoma.

VARIETIES OF PRIMARY CARCINOMA.

There is considerable variety in the forms of carcinoma which may arise primarily in the liver. It will be most convenient to consider seriatim the morbid anatomy of the different varieties.

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* Morley Fletcher: Trans. Path. Soc., vol. l, p. 138.

† Pepper: American Journ. of Med. Sciences, vol. cxxi, p. 287, March, 1901.

‡ Roux: Rev. Med. de la Suisse Romande, Feb. 20, 1897.

I. **Primary Massive Carcinoma (Synonym: Cancer en Amande)** (Hanot and Gilbert).—In this form of primary carcinoma there is a large white or yellowish tumor which expands the liver, like a shell, around it. The surface of the liver is usually smooth; in some cases the growth may project or there may be irregularities from secondary growths; in the latter event there may be adhesions between the liver and adjacent structures, such as the diaphragm, stomach, etc. The growth is more or less localised, and forms a mass as big as a cocoanut or the fœtal head. There may be secondary growths elsewhere in the liver. It usually starts in the right lobe, but in rare instances may be found in the left lobe. According to Eggel, this form is met with in 23 per cent. of the cases of primary carcinoma.

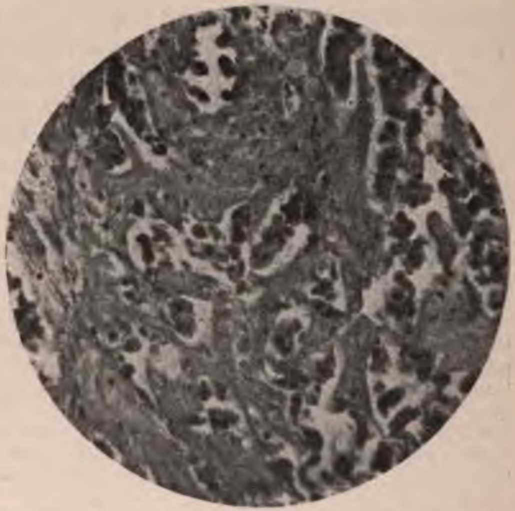

Fig. 58.—Photomicrograph of Section of Diffuse Carcinoma of the Liver.

Shows a large quantity of hyaline fibrous tissue and groups of epithelial cells. (By S. P. Mummery, Esq.) ×15.

Structurally it is usually a polyhedral or spheroidal-celled carcinoma of rapid growth, springing from the liver cells themselves, or possibly from the cubical epithelium of the smaller bile-ducts. It has been suggested that embryonic relics derived from the duodenal diverticulum may be the starting-point of the growth.

Exceptionally the growth is a columnar-celled carcinoma and has then arisen in connexion with the larger intra-hepatic bile-ducts. Hanot and Gilbert[*] figure a giant-celled form of carcinoma in which the largest cells measured as much as 100 μ.

C. Powell White[†] has described a primary carcinoma of the liver which softened down into a large cyst containing straw-coloured fluid; some of the cells measured 30 to 40 μ in diameter. A case of massive carcinoma with much fibrosis resembling a slow-growing carcinoma of the breast is described in the section on Diagnosis (*vide* p. 516). The fibrous tissue showed hyaline change.

II. **Primary Infiltrating or Diffuse Carcinoma.**—In this form the growth is diffuse, and extends more widely than in the previous category. The tumor may be comparatively slow growing and so hard as to simulate cirrhosis. The whole of one lobe may become transformed into a hard yellow growth; in such cases the liver may not be larger than natural.

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[*] Hanot and Gilbert: Études sur les Maladies du foie, p. 30, 1888.

[†] White, C. P.: Brit. Med. Journ., 1899, vol. ii, p. 1347.

Hilton Fagge* described such a case in which the liver weighed 36½ ounces and another weighing 62 ounces, but in his third case it weighed 186 ounces, and in Lee Dickinson's† case, 102 ounces.

It may, however, be rapidly growing and soft, and extend throughout the whole of the liver, uniformly enlarging it.

This was well shown in the liver of a man aged sixty-four which had a uniform hobnail appearance and on section was universally altered. It weighed 151 ounces and microscopically was a rapidly growing spheroidal-celled carcinoma.‡

Structurally, the infiltrating form of carcinoma of the liver is nearly always spheroidal-celled, though a few cases show a transition from a columnar-celled to a spheroidal-celled type. In the hard forms the epithelial cells may be scanty and embedded in wide tracts of fibrous tissue. The fibrous tissue may show advanced hyaline change.

Numerically, this is the rarest form of primary carcinoma of the liver. Eggel estimated that it occurred in 12 per cent. of the cases.

III. **Nodular or Multiple Primary Carcinoma.**—The appearance of the organ is like that seen when it is occupied by secondary growths, the difference being that there is no primary growth. Great care must, of course, be taken to examine every possible situation in the body for a primary growth before admitting that the condition is multiple primary carcinoma of the liver.

The vermiform appendix should always be most carefully scrutinized, for though it is unlikely that secondary growths would occur in the liver while the primary growth in the appendix was so small as to require microscopic examination for its detection and recognition, it is quite conceivable that the primary growth might have been in a vermiform appendix removed for the symptoms of perityphlitis. In cases of primary carcinoma of the vermiform appendix the clinical aspect is that of perityphlitis, and in one case it was only on microscopic examination that the carcinomatous nature was revealed.§

It is quite possible that in some instances multiple adenomata with cirrhosis has been regarded as this form of multiple primary carcinoma, since the naked-eye resemblance is very close. In other cases it is possible that one of the multiple nodules was primary and that the others are secondary, but have grown more rapidly and so come to rival it in size. It is worth while raising the hypothesis that these multiple primary carcinomata may in some instances be multiple growths due to proliferating cells derived from a focus in the mucous membrane of the alimentary canal, which, though irritated, does not show any carcinomatous growth. As an example of "secondary growths without any primary focus" attention may be called to the fact that squamous-celled carcinoma may arise in the inguinal glands of sweeps whose scrota, though covered with warts from the irritation of soot, do not show any definite carcinomatous growth. (Butlin.‖)

This is the most frequent form of primary carcinoma of the liver.

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* Hilton Fagge: Trans. Path. Soc., vol. xxviii, p. 137; vol. xxxi, p. 125.
† Dickinson, L.: Ibid., vol. xlv, p. 87.
‡ Rolleston: Trans. Path. Soc., vol. xlv, p. 92.
§ Rolleston: Lancet, 1900, vol. ii, p. 11.
‖ Butlin, H. T.: Brit. Med. Jour., 1892, vol. i, 1341.

In Eggel's * collection of 163 cases it occurred in 104, or 64.6 per cent., and in about the same proportion in Hale White's † 11 cases from Guy's Hospital, viz., in 6. The multiple tumors grow rapidly, are prone to degenerate, to undergo necrosis, and to become infiltrated with extravasated blood. Histologically, the growth is usually a spheroidal- or polyhedral-celled carcinoma. The cells are often of considerable size, and there is little interstitial connective tissue. The cells are probably derived from proliferation of the hepatic cells. In a few cases the growths are columnar-celled and are in all probability derived from the larger intrahepatic bile-ducts or possibly from mucous glands in their walls.

IV. **Primary Carcinoma Developing in a Cirrhotic Liver** (*Synonyms:* Primary Carcinoma with Cirrhosis; Cirrhosis Maligna; Cirrhosis Carcinomatosa).—This condition was described by Sabourin ‡ under the unfortunate, because confusing, title of Cirrhosis with Multiple Adenomata, and is fully dealt with by Hanot and Gilbert § under the name Carcinoma with Cirrhosis. The latter writers state that a third of the cases of primary carcinoma of the liver are of this special variety. But it is certainly much rarer than that in England, and it is highly probable that more than one condition has been described under this name.

Some of the cases are probably that form of cirrhosis in which the hobnails are extremely well marked, and in which the hepatic cells in them have undergone a compensatory hyperplasia, or cirrhosis with multiple adenomata. This condition of nodular cirrhosis has a great resemblance, naked-eye, to multiple new-growths. The contents of the hobnails may undergo fatty degeneration, and may discharge their contents into the intra-hepatic branches of the portal, or sometimes the hepatic, veins, and give rise to thrombosis; the presence of liver cells in the portal vein has been regarded by some as evidence that the change is carcinomatous, but without sufficient reason. In other cases of cirrhosis it seems probable that thrombosis of the portal vein is the primary factor, and that this leads to fatty degeneration, necrosis, and softening of the cirrhotic hobnails, which thus closely resemble masses of secondary new-growth.

Cirrhosis with compensatory hyperplasia of the liver cells forms a connecting link between cirrhosis, on the one hand, and carcinoma, on the other. Where the line separating the proliferation of the hepatic cells from carcinoma is transgressed, it may be difficult to determine, but that carcinoma may thus result is certainly, though rarely, the case. Many of the cases described as multiple adenocarcinomatous growths associated with cirrhosis are probably rather nodular cirrhosis than malignant, and it is noticeable that in this class secondary growths are very rare. My own impression is that most of the cases are the result of cirrhosis rather than the beginning of carcinoma, but it is advisable to keep an open mind on the subject, as the demarcation between these two conditions is difficult to draw. When secondary growths in the lungs or lymphatic glands are present, as in 3 cases of Hanot and Gilbert's and in cases recorded by Egon Lindner,[*] Travis,[†] and others, the cases must be admitted to be carcinomatous. Well-marked invasion of the veins by growth, when confirmed by the microscope, as has been often done, is also undeniable proof of carcinoma.

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* Eggel: Ziegler's Beiträge, Bd. xxx, S. 506, 1901.
† Hale White: Allbutt's System of Med., vol. iv, p. 205.
‡ Sabourin: Thèse de Paris, 1881; Rev. de Méd., 1884, p. 321.
§ Hanot et Gilbert: Études sur les Maladies du foie, p. 63, 1888.

The relation of the carcinomatous growth to the fibrotic change in carcinoma with cirrhosis has been regarded in various lights. It has been thought:

(*a*) That the cirrhosis and the carcinoma both develop at the same time and are due to irritation applied respectively to the interstitial connective tissue and to the cells of the liver. Hanot and Gilbert, who hold this view, call the condition carcinoma with cirrhosis.

(*b*) That the carcinoma is the primary change, and that the cirrhosis is secondary to the irritation set up by the growth and is related to it in the same way that the interstitial tissue of a hard spheroidal-celled carcinoma is to the epithelial cells. (Lancereaux.[§]) Against this is the fact that secondary growths are commonly present in the liver with little or at the most only local fibrosis around them, while in primary carcinoma with cirrhosis the whole liver, and not merely the parts affected by the growth, is fibrotic.

(*c*) That cirrhosis is the primary change and that the compensatory hyperplasia of the liver cells becomes so excessive and atypical as to pass into definite carcinoma. The history and morbid anatomy of the cases are quite compatible with this view; the duration of the cases is much longer than in other forms of primary malignant disease of the organ; the symptoms are those of cirrhosis, and on examination of the liver after death the cirrhosis is seen to be old and universal, while the carcinoma has the appearances of rapid growth. This view I have long held and is definitely stated by Eggel [‖] from a comprehensive study of the subject.

Since it appears that cirrhosis is the primary change, and that carcinoma supervenes secondarily in much the same manner that carcinoma of the mamma follows chronic mastitis, it would, except for the objection to coining fresh names, be better not to speak of Primary Carcinoma with Cirrhosis, but to alter the title to Primary Carcinoma supervening in a cirrhotic liver, or on the analogy of Paget's disease of the nipple, Cirrhosis Maligna, or on the analogy of carcinoma supervening on a gastric ulcer, to call it Cirrhosis Carcinomatosa.[**]

Morbid Anatomy.—The liver is usually little, if at all, enlarged; but in some instances it may weigh twice its normal amount. It is universally cirrhotic and presents multiple masses of new-growth; one tumor may be so much larger that it would appear to be primary, while the others are secondary. The tumors are often soft or gelatinous, and may be necrotic. The nodules of growth are not umbilicated; this depends on the fact that they contain hardly any stroma, and hence cicatricial contraction, which is at any rate an important factor in the production of umbilication, does not occur. In an early stage the nodules are firm and white; later they degenerate and soften down. They usually project on the surface of the liver, but they may be deeply embedded in its substance. The right lobe is far the most often affected. The growth does not tend to spread by the lymphatics to the glands in the portal fissure.

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[*] Egon Lindner: Wien. klin. Wochen., 1899, S. 1093.

[†] Travis: Johns Hopkins Hosp. Bull., May, 1902.

[§] Lancereaux: Gaz. des Hôp., 1868.

[‖] Eggel: Ziegler's Beiträge, Bd. xxx, S. 506, 1901.

[**] Rolleston: Trans. Path. Soc., vol. lii, p. 203.

The growth has an especial tendency to grow into the portal and hepatic veins and thus spreads through the liver and induces secondary growths. From the portal vein the growth may extend along pervious and dilated veins in the falciform ligament. The portal obstruction induces ascites, which is a constant feature of the disease. Extension into the hepatic vein is not uncommon.

Pennato* describes three varieties of primary carcinoma with cirrhosis, but it seems doubtful whether the distinctions drawn are sufficiently marked to justify this.

The liver nearly always shows adhesions over the capsule. The spleen is enlarged in about half the cases.

Secondary growths are said by Hanot and Gilbert to be as frequent as in other forms of primary carcinoma of the liver. After the liver, they are most frequently seen in the lungs or on the pleura, doubtless from the fact that the growth often extends into the hepatic veins. Secondary growths may also occur on the peritoneum. There is very little tendency to lymphatic infection in this form of primary carcinoma of the liver.

When primary carcinoma supervenes on a cirrhotic liver, the minute structure is nearly always that described by Hanot and Gilbert as trabecular carcinoma. In some instances other histological forms have been met with (Thomson,† Travis ‡), but there is evidently an intimate relationship between trabecular carcinoma and cirrhosis, since its histological characters are not found in other forms of primary carcinoma of the liver.

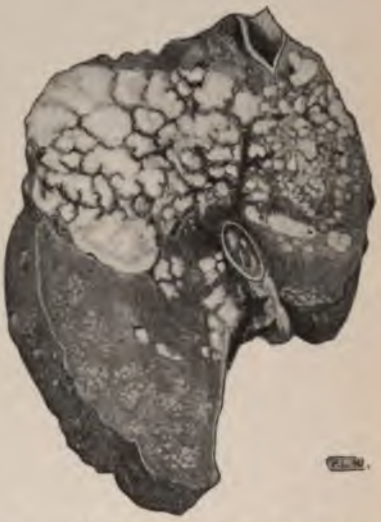

FIG. 59.—SECTION OF THE LIVER IN CARCINOMA WITH CIRRHOSIS.

The growth is seen invading the right lobe and occupying the portal vein. (From case described on p. 478. Drawing by P. L. Mummery, Esq., F. R. C. S.)

Hanot and Gilbert § figure and describe the growth in Primary Carcinoma with Cirrhosis as *Epithelioma trabéculaire*. There are tubular columns of polyhedral or subcolumnar cells arranged in a single layer around a lumen which is usually obliterated, but may contain inspissated bile. The nuclei of the cells are situated externally, at the periphery

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* Pennato: Riforma Medica, May 6, 1897; abstract in Brit. Med. Journ., 1897, vol. ii, Epitome, No. 38.

† Campbell Thomson: Trans. Path. Soc., vol. lii, p. 207.

‡ Travis, C. H.: Johns Hopkins Hosp. Bull., No. 134, p. 108, May, 1902.

§ Hanot and Gilbert: Études sur les Maladies du foie, p. 41, 1880.

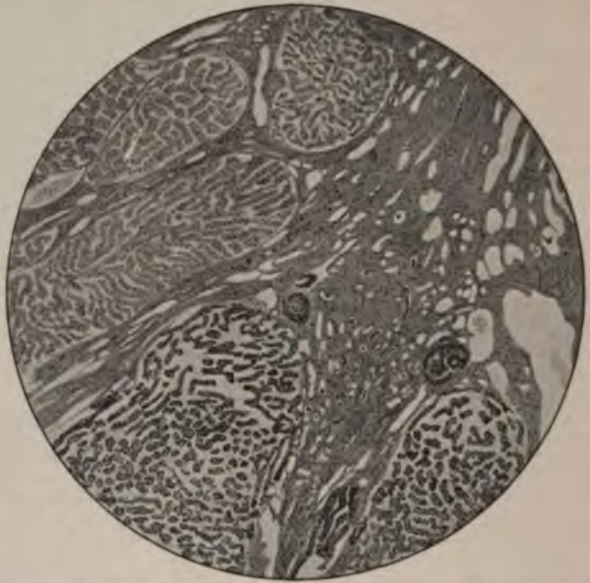

FIG. 60.—SHOWS MICROSCOPIC APPEARANCES IN CARCINOMA WITH CIRRHOSIS. CIRRHOSIS TO THE LEFT, CARCINOMA TO THE RIGHT. UNDER A VERY LOW POWER.*

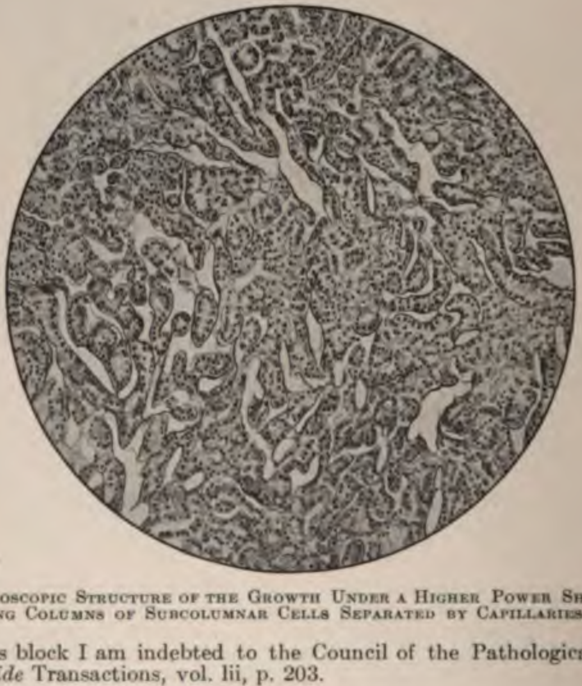

FIG. 61.—MICROSCOPIC STRUCTURE OF THE GROWTH UNDER A HIGHER POWER SHOWS BRANCHING COLUMNS OF SUBCOLUMNAR CELLS SEPARATED BY CAPILLARIES.

*For this block I am indebted to the Council of the Pathological Society of London. *Vide* Transactions, vol. lii, p. 203.

of the tubular column. These columns branch, undulate, and twist, and are separated from each other by capillaries which may contain blood. Except for the capillary walls and occasionally well-formed venules, there is no intertubular stroma. The cells stain well, like the pseudobiliary canaliculi, and are smaller than liver cells, being intermediate in size between them and the cells of the pseudobile canaliculi. Occasionally multinuclear cells are present. Both the growths in the liver and the secondary growths in the lung have been known to show bile-stained contents.[*]

The carcinomatous growth may be derived from the liver cells directly or may supervene on the hyperplasia of the hepatic cells, which occurs as a compensatory change in cirrhosis and leads—(i) to the formation of multiple adenomata in cirrhosis (*vide* p. 456) and (ii) to the production of the pseudobile canaliculi in the interlobular connective tissue.

Hanot and Gilbert[†] and Hunter[‡] describe the direct transformation of the liver cells into carcinoma. Schmieden[§] has traced the commencement of carcinoma in the centre of multiple adenomata in a cirrhotic liver, and it seems highly likely that multiple adenomata might be an antecedent stage to carcinoma.

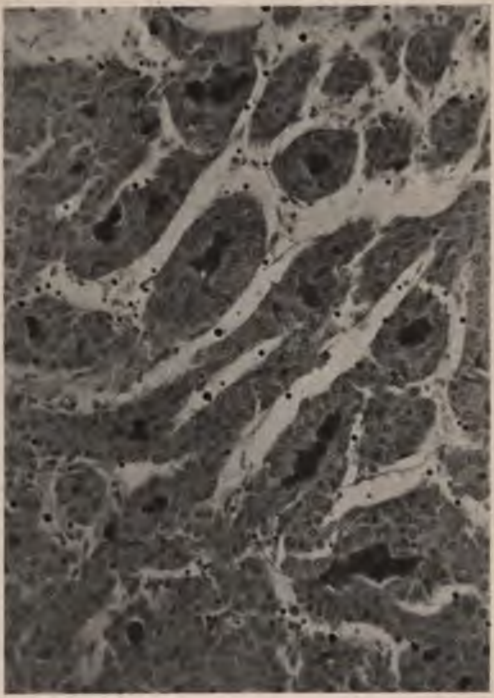

FIG. 62.—PHOTOMICROGRAPH OF CARCINOMA WITH CIRRHOSIS. SHOWING TUBULAR COLUMNS OF CELLS ENCLOSING MASSES OF INSPISSATED BILE.

In the capillaries separating the columns of cells a few leucocytes are seen. (Dr. H. Spitta.) × 220.

In some cases the trabecular carcinoma may be a further development of the pseudobile canaliculi, which were shown years ago by Dreschfeld[‖] to be due to rapid proliferation of the liver cells and may be regarded in the light of a compensatory hyperplasia (Hanot[**]). The development of carcinoma might be considered as an outcome of the habit of proliferation which began as a compensatory process, but, like endarteritis, must be considered as a compensatory mechanism which has failed.

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[*] Cloin: Prag. med. Wochen., Bd. xxvi, S. 261, 1901.
[†] Hanot and Gilbert: Études sur les Maladies du foie, p. 41.
[‡] Hunter, W.: Brit. Med. Journ., 1901, vol. i, p. 151.
[§] Schmieden: Virchow's Archiv, Bd. clix, S. 290.
[‖] Dreschfeld: Journ. of Anat. and Physiolog., London, vol. xiv, p. 69.
[**] Hanot: Gaz. des Hôp., Paris, July 10, 1896.

When the growth is compressed or under pressure, the capillary walls may collapse and the structure of the growth is obscured. Degeneration of the cells may occur; the growth may become infiltrated with blood or invaded by fibrosis.

The clinical aspects of carcinoma with cirrhosis are practically the same as those of portal cirrhosis. It is only when the liver is large that nodules can be felt; as a rule, the liver is small. Ascites is constant, while jaundice and pain in the hepatic region are said to be more prominent than in simple cirrhosis. Carcinoma with cirrhosis occurs, as would naturally be expected from the greater incidence of cirrhosis in men, very much more frequently in the male than in the female sex. In 22 recorded cases of which I have notes all were in men.

The following case was an example of carcinoma with cirrhosis*:

A Scotchman aged forty-four, who had taken alcohol and neat whisky, but not in great excess, was under my care in St. George's Hospital July–October, 1900. For four months before death his abdomen had been swollen; about three months before death he had hæmatemesis and melæna on two occasions. During August and September paracentesis was performed four times. A month before death he became comatose, but revived after saline intravenous transfusion. There was a good deal of pain in the hepatic region. His facial aspect was that of cirrhosis; there were distended abdominal veins, but neither the liver nor spleen could be felt. The case was regarded as one of cirrhosis, complicated, since paracentesis was required four times, by chronic peritonitis. At the necropsy the liver (*vide* Fig. 59) weighed 52 ounces and was markedly cirrhotic and hobnailed. On the convexity of the right lobe, close to and involving the attachment of the falciform ligament, there was a soft, whitish projection which invaded the liver for a rather greater extent than it projected above its surface, and was about the size of an orange. On section, it was gelatinous and passed by continuity into the bifurcation of the portal vein blocking up its trunk and its intra-hepatic branches, thus giving rise to secondary growths in the liver. The walls of the portal vein were thickened. The falciform ligament contained a large vein the size of a crow's quill, filled with growth.

Microscopically the liver showed multilobular cirrhosis with extensive pseudobile canalicular formation. In the region showing new-growth to the naked eye there was a formation composed of columns of cells without any lumen. The columns twisted and curled about and were like, though larger than, pseudobile canaliculi. This appearance corresponds with trabecular carcinoma described by Hanot and Gilbert. The growth in the portal vein was of the same nature and infiltrated the walls of the vein, which, in addition, showed endophlebitis and secondary calcification.

The gall-bladder was adherent to the pylorus by old adhesions; it contained small bilirubin calculi; there was no growth in it.

The bile-ducts were pervious. The veins at the lower end of the œsophagus were dilated, as were those under the peritoneum. The stomach showed very marked chronic gastritis. There was no primary growth in the pancreas, intestine, or other part of the body. The spleen (16 ounces) was enlarged, firm, and showed perisplenitis and the scar of an old infarct. Except for slight thickening of the capsule of the liver and perisplenitis, there was no chronic peritonitis. No tubercle was found in the body.

V. **Primary Melanotic Carcinoma.**—Two cases have been recorded by competent observers in which it appeared that there was a primary melanotic carcinoma of the liver. The subject is one of great pathological interest and has given rise to a good deal of discussion. In both cases an eye had been removed, in one for glaucoma, in the other for a sarcoma.

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* Rolleston: Trans. Path. Soc., vol. lii, p. 203.

Hale White's[*] case of primary melanotic carcinoma of the liver was in a man aged sixty-six whose eye, removed for glaucoma one year before, showed no sign of malignant disease. Fisher and Box's[†] case of multiple melanotic carcinoma of the liver (which weighed 12 pounds 6 ounces), bones, lungs, and heart in a man who had had an eye removed for melanotic sarcoma fourteen years before may be mentioned in connexion with the occurrence of primary melanotic carcinoma in the liver. It is therefore open to question whether the growths were really primary in the liver; probably many would regard the growths as endotheliomata rather than carcinomata.

General Remarks on the Pathology of Primary Carcinoma of the Liver.

Starting-point of Carcinoma.—Primary carcinoma may arise from proliferation of the liver cells, of the cubical epithelium of the small bile-ducts, or of the columnar epithelium of the larger intra-hepatic bile-ducts. The liver cells are more frequently the origin of carcinoma than are the cells of the bile channels—according to Pepere,[‡] in the proportion of 7 to 1. Spheroidal-celled carcinoma may be derived from the liver cells or from the small bile-ducts; the larger-celled growths are probably derived from the liver cells. Hanot and Gilbert[§] believed that the trabecular form of carcinoma, seen in carcinoma with cirrhosis, is derived from the liver cells. My own belief is that it may be directly derived from the pseudobile canaliculi or so-called new bile-ducts. The latter are produced by proliferation of the liver cells as an attempt at compensation.[‖] Columnar-celled growths are derived from the larger intra-hepatic bile-ducts or possibly from mucous glands in their walls.

In addition to the normal tissues of the liver it is, in accordance with Cohnheim's theory, conceivable that carcinoma might arise in pieces of other abdominal organs which have become included in the liver as the result of some irregularity in the process of development. It has been suggested that embryonic relics of the duodenal diverticulum might persist and be the starting-point of a carcinoma, or that a small piece of pancreas (Pepere[**]) or an accessory suprarenal gland might be included in the liver. The question is interesting, but except for the origin of primary malignant tumors of the liver from included accessory suprarenal gland, there is little but theory to go on.

Schmorl[††] and other writers have established the fact that accessory suprarenal bodies may occur in the liver. The development of a malignant disease in the liver from an included accessory suprarenal body or "rest" is analogous to the well-known malignant renal tumors arising in suprarenal "rests." Some doubt might arise as to the proper designation of such a tumor (hepatic hypernephroma), but inasmuch as they resemble carcinoma, they may be tentatively referred to here, though some writers might prefer to class them with the endotheliomata or peritheliomata. Pepere[‡‡] has given an elaborate account of a primary malignant tumor of the left lobe of the liver arising in a suprarenal "rest," which appears to be the first recorded case of this kind.

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[*] Hale White: Trans. Path. Soc., vol. xxxvii, p. 272.

[†] Fisher and Box: Brit. Med. Journ., 1900, vol. i, p. 639.

[‡] Pepere: I Tumori maligna primarii del Fegato, p. 171, 1902.

[§] Hanot et Gilbert: Etudes sur les Maladies du foie, p. 41, 1888.

[‖] Rolleston: Trans. Path. Soc., vol. lii, p. 203.

[**] Pepere: Arch. per le Sc. Med., vol. xxvi, p. 148, 1902.

[††] Schmorl: Beiträge z. path. Anat. u. z. allg. Path., Bd. ix, S. 523.

[‡‡] Pepere: Archiv. de Méd. expériment. et d' Anat. path., tome xiv, p. 763, 1902.

Degenerative Changes in the Tumor.—Necrotic changes are not uncommon, while the epithelial cells often show fatty change; but, probably owing to rapid growth, colloid degeneration is not met with. From extensive necrosis the growth occasionally shows cystic change and some hæmorrhage may take place. The fibrous tissue may undergo widespread hyaline change.

The Incidence of Secondary Growths in Primary Carcinoma of the Liver.—Secondary growths are common in the liver, and, contrary to what might be expected and is indeed sometimes stated, are found in other situations in more than half the cases. In Eggel's * collection metastasis occurred outside the liver in 66 per cent. Secondary growths are most frequent in the immediate neighbourhood; thus infection may spread by the lymphatics to the glands in the hilum, which are often enlarged and may exert pressure on the portal vein and bile-ducts. Lymphatic glands elsewhere, in the upper part of the abdomen and in the thorax, may be infected. Metastasis also occurs by the blood-stream; the growth may extend directly into the portal and hepatic veins, and thus give rise—(i) to fresh growths in the substance of the liver and (ii) by embolic masses of growth which pass *via* the hepatic veins to set up secondary nodules in the lungs.

In 21 cases of primary carcinoma of the liver Lancereaux † found growths four times in the gall-bladder and twice each in the peritoneum, the lungs, and the spleen.

In cases of primary carcinoma supervening in a cirrhotic liver the secondary growths in the lungs sometimes show bile-pigment. (Heller,‡ Cloin.§)

Extension of the primary hepatic growth into the portal or hepatic veins is much commoner in the special form of carcinoma with cirrhosis than in the other varieties of primary carcinoma. The growth in the vein may lead to very considerable dilatation of its walls, so that it is difficult to make out the exact limits of the vein in the substance of the liver.

In comparing renal and hepatic new-growths as regards their mode of extension, it may be pointed out that one mode of extension, viz., along the excretory duct, is extremely rare in malignant disease of the liver. Gilbert and Claude ‖ have recorded a case, which they believed to be unique, of extension of a massive carcinoma of the right lobe of the liver into the common bile-duct which set up obstinate jaundice.

Incidence of Gall-stones in Primary Carcinoma of the Liver.—Although gall-stones occur in a high percentage—80–90 per cent.—of cases of primary carcinoma of the gall-bladder, it is generally believed that there is no special relationship between cholelithiasis and primary carcinoma of the liver itself, and that gall-stones are merely a coincidence in malignant disease of the liver. Confusion has existed in the past, and primary carcinoma of the gall-bladder has sometimes been described as primary carcinoma of the liver, so any statistics, like some of my own, in which there is a high percentage of gall-stones in primary carcinoma, must be carefully criticised from this point of view.

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* Eggel: Ziegler's Beiträge, Bd. xxx, 1901.

† Lancereaux: Traité des Maladies du foie et du Pancreas, p. 472, 1899.

‡ Heller: Centralbl. f. allg. Path., Oct. 15, 1896.

§ Cloin: Prag. med. Wochen., Bd. xxvi, S. 261, 1901.

‖ Gilbert and Claude: Archiv. gén. de Méd., t. clxxv, 1895, p. 513.

Voelcker, at a meeting of the Pathological Society of London, on Nov. 15, 1898, said that he had examined 9 cases of primary carcinoma of the liver, in none of which were any gall-stones present. In twenty-one and a half years, at St. George's Hospital, there were 18 cases regarded as primary carcinoma of the liver, about two-thirds of which I saw or examined myself; four of these, or 22.2 per cent., contained calculi in the gall-bladder.

Varieties of Primary Sarcoma.

I. **Primary Massive Sarcoma.**—There is a large tumor, usually in the right lobe, which is analogous to the massive form of primary carcinoma (p. 471). There may be secondary tumors in other parts of the liver, but from their relative size there is no doubt as to which is the primary growth. In some instances the growth may project from the under surface of the liver so as to become pedunculated. A fair proportion, probably about one-third, of the cases of primary sarcoma belong to this group.

In 44 cases tabulated by Pepere * 14 were in this category.

The cells may be small, round, spindle, or of various shapes and sizes; sometimes, especially when growth is rapid, multinuclear giant-cells are present. Hæmorrhage frequently takes place into the growth and gives rise to a mottled or red appearance. The growths frequently have a spongy aspect on section. Large sarcomatous tumors may be very hæmorrhagic and break down into cystic cavities and even imitate abscesses.

A case recorded by Bramwell and Leith† simulated an abscess; aspiration was performed three times, with removal of 123 ounces of anchovy coloured fluid.

In a woman aged sixty-four under the care of my colleague, Dr. Penrose, there was a large cystic tumor continuous with the right lobe of the liver and reaching down to the iliac crest. It was explored by Mr. Turner, and a large quantity of blood-stained fluid and a little growth removed; it was thought possible that it was a pancreatic cyst, but the fluid contained nothing but altered blood and had none of the characters of the fluid in a pancreatic cyst. Microscopically the growth was a mixed-celled sarcoma. Subsequently the patient died of bronchitis. At the necropsy there was an enormous cystic tumor, still containing brown, blood-stained fluid, projecting from the portal fissure and carrying the cystic and common bile-ducts and portal vein in front of it. There was, however, no jaundice or ascites. There were secondary growths in the retroperitoneal glands and in the lungs.

II. **Nodular, or Multiple, Primary Sarcoma.**—There are a number of discrete nodules scattered in the substance of the liver which are so much of the same size that no individual nodule can be regarded as primary and antecedent to the others. This appears to be the most frequent anatomical form of primary sarcoma. It was present in 18 out of 44 cases of primary sarcoma tabulated by Pepere. Where the nodules are small and very numerous, they tend to become confluent and to produce either a massive growth, like the form just described, or a more diffuse infiltration, in which the cut surface has an appearance not unlike granite.

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* Pepere: I Tumori maligni primarii del Fegato, p. 118, Napoli, 1902.

† Bramwell and Leith: Lancet, 1897, vol. i, p. 170.

Structurally, the cells of the growth may be of very various types—spindle, round, irregular, or giant-cells.

There is a good example of a multiple primary spindle-celled sarcoma of the liver in the museum of the Royal Free Hospital. The late Miss Mabel Webb, M.B., curator of the Museum, kindly gave me a slide from this case which is reproduced below (Fig. 63).

III. **Diffuse or Infiltrating Primary Sarcoma.**—Sarcoma may uniformly infiltrate both lobes of the liver. This form is not infrequently seen in very early life, and must be carefully distinguished from the changes due to congenital syphilis. Some of the hard infiltrating growths, formerly spoken of as "scirrhus" of the liver, belong to this category, since they show a structure like that of an endothelioma. There are large endothelial cells and large quantities of hyaline fibrous tissue.

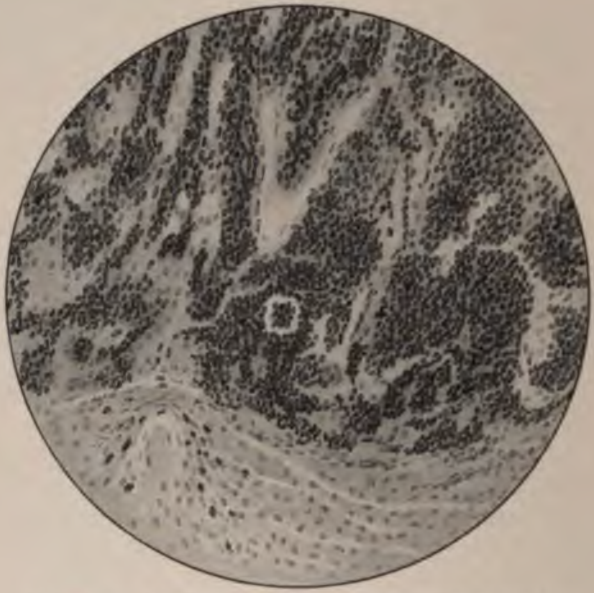

FIG. 63.—DRAWING OF A SMALL SPINDLE-CELLED SARCOMA.
The liver tissue which is being invaded is very lightly stained.

IV. **Sarcoma Arising in a Cirrhotic Liver.**—This development of primary sarcoma in a cirrhotic liver corresponds to carcinoma with cirrhosis; in the former the hyperplasia of the connective tissues has gone on to embryonic connective-tissue (sarcoma) formation, while in the latter the compensatory proliferation of the liver cells has become atypical and carcinomatous. Primary sarcoma has as yet only been described as arising in a cirrhotic liver in two cases, viz., by Ford,[*] and by Vecchi and Guerrini.[†]

W. W. Ford described a remarkable case of primary sarcoma, forming a tumor 5 by 8 cm., developing in a highly cirrhotic liver. This growth, which was friable, was composed of spindle- and round-cells and had produced secondary growths on the peritoneum. There was ascites. The patient, an alcoholic male aged fifty-nine, died from cerebral hæmorrhage.

V. **Primary Melanotic Sarcoma of the Liver.**—I have references to 8 published cases,[‡] but it is doubtful whether they are genuine and not secondary to a small growth in the uveal tract or in a cutaneous mole which has been overlooked. As shown by Dr. Pitt's case (*vide* p. 498), a very minute growth in the uveal tract, which escapes ophthalmoscopic examination and gives rise to no symptoms during life, may produce great enlargement of the liver. Thus no case can be accepted unless it is clear that the eyes were specially examined after death, and this does not appear to have been done. In the recorded cases the most that can be found about the eyes is that there were no symptoms during life.

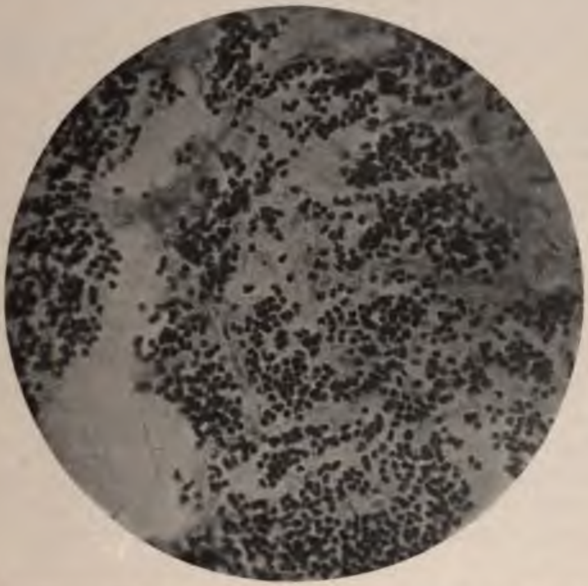

FIG. 64.—PHOTOMICROGRAPH SHOWS THE EDGE OF A SMALL ROUND-CELL SARCOMA INFILTRATING THE LIVER DIFFUSELY IN AN INFANT.
The growth was primary in the liver. (By S. G. Penny, Esq.) × 200.

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[*] Ford, W. W.: American Journal of the Medical Sciences, vol. cxx, p. 43, Oct., 1900.

[†] Vecchi and Guerrini: La Riforma Med., tome xvii, 1901.

[‡] Frerichs: Diseases of the Liver, vol. ii, p. 326. Transl. New Sydenham Soc. Block, O. C.: Archiv der Heilkunde, Bd. xvi, S. 412, 1875. Legg, W.: St. Bartholomew's Hosp. Reports, vol. xiii, p. 160, 1877. Delépine, S.: Trans. Path. Soc., vol. xlii, p. 161. Penrose, F. G.: Trans. Path. Soc., vol. xlii, p. 172. Middlesex Hospital Reports, 1891, p. 278. Holsti: Brit. Med. Journ., 1895, vol. ii, epitome No. 395. Belin: France Médicale, 1887.

STARTING-PLACE OF SARCOMA.

Sarcoma may arise primarily from the general connective tissue of the liver in the portal spaces, from the perivascular connective tissue, from Kupffer's star-like cells around the capillaries, and from the endothelium of the blood-vessels and lymphatics. The growths arising from the tissues of the vessels, angiosarcomata, may be further divided into—(i) those arising from the lining endothelium of the blood or lymphatic vessels, the endotheliomata, and (ii) those arising from the perivascular sheaths formed of endothelium covering the vessels externally, the peritheliomata. Probably a large proportion of the primary growths usually classed as sarcoma of the liver belong to the angiosarcomata.

Among 44 cases of primary sarcoma of the liver tabulated by Pepere[*] 22 were regarded as derived from the vessels, and of these, 11 were endotheliomata and 8 peritheliomata.

As already mentioned, sarcoma has been found to arise in the proliferation of the interstitial tissue of a cirrhotic liver. (W. W. Ford[†]; Vecchi and Guerrini.[‡])

Microscopically there is a general tendency for sarcoma in the liver to assume an alveolar arrangement and so to imitate carcinoma; it is, indeed, not unlikely that some cases of large or medium-sized round-celled sarcomata of the liver have been described as carcinomata, as there is often considerable difficulty in coming to a satisfactory decision as to the nature of the growth in such cases. One reason why a sarcoma is often alveolar is that the growth is an endothelioma, derived from the endothelium lining the small blood-vessels or lymphatics.

The forms of sarcoma met with are very various—small round-celled, large round-cell, spindle-celled, irregular-celled sarcoma with giant-cells, lymphosarcoma, angiosarcoma, including under this head the endotheliomata, and melanotic sarcoma, have all been described.

Condition of the Remainder of the Liver in Primary Malignant Disease.

There may, of course, be secondary growths in parts of the liver remote from the main tumor. In some cases compensatory hyperplasia of the liver cells may form nodules which are with difficulty distinguished from secondary growths. Local venous engorgement from pressure on the trunks of the intra-hepatic veins or local bile-staining from compression of the bile-ducts may also be met with. The occurrence of cirrhosis has already been dealt with. As a curiosity, the association of primary malignant disease of the liver with calcified hydatid cysts in the organ may be mentioned.[§]

Growths in the liver may become invaded by micro-organisms; this may occur during life and give rise to suppuration. It is not uncommon for micro-organisms

[*] Pepere: I Tumori maligni primarii del Fegato, p. 118, 1902.
[†] Ford, W. W.: American Journ. Med. Sciences, vol. cxx, p. 43, Oct., 1900.
[‡] Vecchi and Guerrini: La Riforma Med., tome xvii, 1901.
[§] St. Thomas' Hospital Reports, vol. xxix, p. 141.

to gain access to the growth at or after death; they are then of no importance. Hebb [*] found long bacilli in a case of primary carcinoma and Delépine [†] staphylococci in primary melanotic sarcoma of the liver.

Secondary Malignant Disease of the Liver.

INCIDENCE.

Numerical Ratio Between the Incidence of Secondary and Primary Malignant Disease of the Liver.—Secondary malignant growths in the liver are very common, while primary growths of the liver substance are rare. The numerical relationship between primary and secondary malignant disease of the liver is often stated to be about 1 to 20. Even this is rather overstating the frequency of primary malignant disease of the liver. Possibly cases of malignant disease of the gall-bladder or larger bile-ducts have been regarded as primary in the liver by some observers and so have tended to vitiate statistics.

Hale White [‡] puts the proportion of undoubted primary to secondary carcinoma as 1 to 25. He found that primary malignant disease was the cause of death in 0.1 per cent., and that secondary growths were present in 3 per cent. of patients examined after death at Guy's Hospital.

Hansemann, [§] in twenty years,—1870–1889,—found that 258 autopsies showing malignant disease in the liver had been performed in the Pathological Institute at Berlin. Of these, 25 were primary in the gall-bladder, 2 in the larger ducts, and either 6 or 4 primary in the liver. This shows a ratio of primary to secondary growths of nearly 1 to 40.

Incidence of Secondary Carcinoma and Sarcoma in the Liver.—Secondary carcinoma is far more often met with than secondary sarcoma.

In 100 cases of secondary malignant disease of the liver abstracted from the postmortem records of St. George's Hospital, 77 were carcinoma and 23 sarcoma. The cases of sarcoma include endotheliomata, such as the malignant tumors of the suprarenal body, of which there were 5. There were 3 cases of melanotic sarcoma. In Hale White's [‖] figures the percentage was 92.65 carcinomatous, and 7.35 sarcomatous, secondary growths. In his 136 cases of secondary growths in the liver at least 126 were carcinomatous.

The smaller incidence of secondary sarcoma in the liver is readily explained not only by the fact that carcinoma is a commoner growth than sarcoma, but also by the infrequency of primary sarcoma in the alimentary canal, or, in other words, within the territory of the portal vein. Sarcoma, like pyæmia, travels by the veins to and through the lungs, which tend to filter out the micro-organisms or infecting cells and thus at their own expense protect the rest of the body.

Sex.—Secondary malignant disease of the liver is rather more frequent in women than in men.

During the four years—1897–1900—there were, according to the registrar-general's returns for England and Wales, 8654 female and 5532 male deaths from malignant disease of the liver; though these figures include malignant disease of the gall-bladder, which is much commoner in women, it is probable that they rep-

[*] Hebb, R. G.: Westminster Hospital Reports, vol. iii, p. 180.

[†] Delépine, S.: Trans. Path. Soc., vol. xlii, p. 161.

[‡] Hale White: Allbutt's System, vol. iv, p. 204.

[§] Hansemann: Berlin. klin. Wochen., 1890, S. 353.

[‖] Hale White: Allbutt's System of Med., vol. iv, p. 194.

resent very fairly the incidence of secondary malignant disease and correspond with Hale White's* estimate of 4 to 3.

The greater frequency of secondary malignant disease of the liver in women depends not only on the greater incidence of malignant disease in that sex, but also on the special predominance of malignant disease of the mamma and female genital organs. Secondary growths in the liver often follow cancer of the mamma and genital organs, but rarely occur in malignant disease of lip, mouth, and tongue, which are much commoner in the male than in the female sex.

Payne's statistics † show that the incidence of cancer generally, and especially of the alimentary canal, is absolutely and steadily increasing. According to the registrar-general's statistics, although at the present time women suffer more severely from malignant disease than men in the aggregate, the incidence of malignant disease has increased more rapidly among men than in the other sex. It is, therefore, highly probable that secondary malignant disease of the liver is becoming more frequent in males than formerly.

In 100 cases of secondary malignant disease of the liver examined at St. George's Hospital and taken in continuity from the postmortem records, 1892–1902, I was surprised to find that the number of males (66) were nearly double that (34) of the females.

Age.—Secondary malignant disease of the liver occurs most frequently after forty years of age.

The average age of 100 cases of secondary malignant disease of the liver examined at St. George's Hospital was 49.8 years. The average ages of the 66 males was 51.3 years, and of the 34 females, 47 years.

The average age is, as might be expected, higher in the cases of secondary carcinoma than in those of secondary sarcoma.

Among 100 cases of secondary malignant disease of the liver the average age of 77 cases of carcinoma was 51.9 years (50 males cases, average age, 53.1 years; 27 female cases, average age, 48.5); while the average age of 23 cases of secondary sarcoma was 43 years (16 males, 43.8 years; 7 females, 41.1).

Probably the earliest recorded case of secondary carcinoma of the liver is Zuppinger's,‡ in a girl aged twelve years. The primary growth was a columnar-celled carcinoma of the sigmoid flexure.

MORBID ANATOMY AND HISTOLOGY.

The liver is sometimes of the normal size, with a few secondary growths scattered over its surface. Often, however, the secondary growths in the liver increase very rapidly, and if the primary growth in the alimentary canal is comparatively stationary, the liver may reach a very large size. In cases, such as carcinoma of the breast or melanotic sarcoma of the uveal tract, where the primary growth may have been removed after infection of the liver has actually taken place, the liver may subsequently become greatly enlarged. The largest livers known occur in secondary malignant disease. Hilton Fagge * mentions a liver weighing 28 pounds, and Litten described a case of secondary melanotic sarcoma in which the liver weighed 27 pounds.

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* Hale White: Allbutt's System, vol. iv, p. 197

† Payne, J. F.: Lancet, 1899, vol. ii, p. 765.

‡ Zuppinger: Wien. klin. Wochen., April 26, 1900, S. 389.

Secondary invasion of the liver is hardly ever limited to a single nodule of growth. The liver may show a number of multiple and discrete growths, or may be widely and diffusely infiltrated for a greater or less extent. The latter condition is sometimes well seen in carcinoma of the breast or in melanotic sarcoma. When widely infiltrated, the liver is enlarged, but preserves its general shape and anatomical outlines very fairly.

"Farre's tubercles" was formerly a well-known synonym for secondary growths in the liver. This writer described "Tubera circumscripta" and "Tubera diffusa," corresponding to the two forms mentioned above.†

In some instances nodules originally separate may unite and form a large irregular mass. The growths are scattered throughout the liver, but are especially frequent near the surface of the organ, and are rarely seen on section when entirely absent from the surface. They grow rapidly and receive their blood-supply from the hepatic artery, which is sometimes considerably enlarged.

In this connexion it is interesting to refer to a plate of Bright's ‡ showing a large artery supplying a mass of secondary new-growth.

Whether carcinomatous or sarcomatous, the naked-eye appearances of the nodules have much in common. They are usually white in colour, and are not infrequently bile-stained and may be speckled with blood or extremely hæmorrhagic. In secondary melanotic sarcoma there may be isolated pigmented nodules, areas of diffuse melanotic infiltration, or both combined. In some cases the secondary melanotic growths are almost or quite devoid of pigment, at any rate to the naked eye. Sarcomatous growths are more likely to be hæmorrhagic and to form softened pseudo-cysts; as a rule, they are not depressed in the centre or umbilicated, a change often seen in secondary carcinomatous growths on the surface of the liver. It has been said that secondary sarcomatous nodules are never umbilicated, and may thus be distinguished from secondary carcinomatous growths in the liver. This is too dogmatic a statement and must admit of some exceptions.

In St. Bartholomew's Hospital Museum there is the liver of a boy aged ten years enormously enlarged and studded with umbilicated nodules secondary to sarcoma of the kidney (No. 2215 c).

The dead-white colour of some secondary carcinomatous nodules, especially columnar-celled growths, may give rise to an appearance very like a gumma, so that considerable difficulty may arise in distinguishing between the two conditions, especially when only a limited examination can be made, as at exploratory laparotomies.

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* Fagge: Principles and Practice of Medicine, vol. ii, p. 296, 1886.
† J. R. Farre: Morbid Anatomy of the Liver, 1815.
‡ Bright: Guy's Hospital Reports, vol. i, p. 638, 1836.

I have several times examined fragments removed during life which have turned out to be columnar-celled growths secondary to a latent carcinoma in the stomach or colon and which it was naturally hoped might be gummata. Gouget * described a columnar-celled carcinoma of the liver which was at first regarded as a gumma.

The consistency of the growths varies considerably. Diffuse areas of infiltration may be hard, but as a general rule the larger the size of a secondary growth, the softer it is, since degeneration and necrotic changes are more prone to supervene than in smaller nodules. Small discrete nodules cut with the same kind of resistance as a cream cheese.

Degenerative Changes.—The central parts of the larger nodules readily undergo fatty degeneration or necrosis and may have a caseous or softened appearance. I have seen a rapidly growing mass of carcinoma present the honeycombed and softened appearance of actinomycosis. Extreme softening may in some instances be due to suppuration from infection. The necrosed portions may be yellow or green from bile-staining, or may become infiltrated with blood. This hæmorrhagic condition is more often seen in sarcoma, but it may also be met with in secondary carcinomatous growths. Sometimes the hæmorrhage into the degenerated growth is so profuse as to lead to serious syncope, but when this occurs, the growth has usually ruptured and allowed blood to pass into the peritoneal cavity. In other instances a sanguineous ascitic effusion is due to comparatively insignificant leakage from a small nodule.

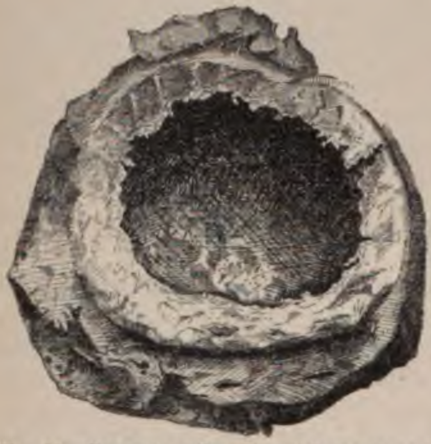

Fig. 65.—Drawing of Cyst Due to Softening of a Secondary Carcinomatous Growth in the Liver from a Specimen in St. George's Hospital Museum. (Series IX, 184 L.) (Drawn by L. Jones, Esq., M.B., F.R.C.S.)

Colloid degeneration rarely occurs in a secondary growth in the liver.

There is a good specimen of a mass of colloid carcinoma, the size of a man's fist, in St. Bartholomew's Hospital Museum, secondary to a growth in the rectum. (No. 2216 H.)

According to Schueppel,† diffuse colloid cancer of the peritoneum may spread by the lymphatics of the capsule of the liver and pass into its substance like strings. Eventually a whole lobe of the liver may become transformed into a colloid mass.

Myxomatous and hyaline degeneration may attack the fibrous tissue of a slow-growing secondary nodule of carcinoma, or occur in secondary endotheliomatous nodules even though growing rapidly.

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* Gouget: Bull. Soc. Anat. Paris, 1890, p. 605.

† Schueppel: v. Ziemssen's Cyclopædia of Practical Medicine, vol. ix, p. 338. English trans.

Formation of Pseudo-cysts.—Degeneration and softening of secondary malignant growths may lead to the formation of definite cysts. This may occur in any form of carcinoma, even in the squamous-celled variety, and in sarcomata. It is, however, a rather rare condition.

In a case of carcinoma of the stomach recorded by Hawthorne * there were numerous cysts in the right lobe of the liver, due to softened new-growth; the largest had a diameter of 4½ inches. Aspiration during life resulted in the withdrawal of 58 ounces of blood-stained fluid. The case imitated an abscess.

In a case of carcinoma of the pylorus recorded by Nicaise † the liver, which weighed 75 ounces and contained numerous secondary growths, had a tongue-shaped lobe with a hæmorrhagic cyst due to destruction of the growth.

In a case of carcinoma of the liver probably secondary to the pancreas in a man aged fifty-one under Dr. Sainsbury's care there were numerous cystic spaces with caseous contents. Microscopically the growth was a carcinoma, showing a transition from a columnar to a spheroidal type, with a considerable amount of fibrous tissue and extensive necrotic and cystic changes. The liver is in the Museum of the Royal Free Hospital, and by the courtesy of the late Miss M. Webb, M.B., Curator, I was enabled to cut sections of the growths.

Voelcker ‡ described secondary squamous-celled carcinomatous nodules with cystic change, a smooth thin layer of new-growth alone being left as the wall of the cyst. Thomson § met with a similar case where the cyst-wall could easily be peeled out of the liver; it closely resembled an hydatid cyst and contained clear yellow fluid. There is a somewhat similar specimen with cysts the size of a mandarin orange in St. Bartholomew's Hospital Museum secondary to a growth in the œsophagus. In a case described by Sharkey ‖ the liver was studded with cysts lined by squamous epithelium.

In St. Bartholomew's Hospital Museum there is a specimen (2215E) of secondary sarcomatous growths in the liver which have broken down so extensively that the appearance is not unlike that of cystic disease of the organ in the adult; the primary growth was in the skin of the back. I have seen the same thing in a secondary endothelioma of the liver which weighed 18 pounds, the primary growth being in the left kidney. (*Vide* p. 517.)

Umbilication.—Not uncommonly nodules of secondary growth on the surface of the liver show a central depression or cupping which is spoken of as umbilication. It occurs in comparatively slow-growing carcinomatous nodules and is very rare in secondary sarcoma. (*Vide* p. 487.)

This umbilication is due to the cells in the central part of the nodule undergoing degeneration and becoming compressed by the surrounding fibrous tissue, which, from the greater age of the growth in the centre, is better developed than in the more recent peripheral parts of the nodule. Another factor is the more exuberant cellular proliferation at the edge of the nodule, which leads to a heaping-up of growth. The depression of the oldest part of an oyster's shell, viz., that near the hinge, illustrates the production of umbilication. (Wilks.**) Umbilication is often absent in rapidly growing nodules of small size.

Growths in the liver frequently press on the branches of the portal vein and may thus help to cause ascites; pressure on the hepatic veins is often seen, and gives rise to local chronic venous engorgement. In a certain number of instances the secondary growths project into the veins and set up thrombosis; detachment of small pieces of growth projecting into the lumen of the hepatic veins leads to secondary growths in the lungs. Occasionally a secondary growth may form a polypoid mass in the hepatic or portal veins.

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* Hawthorne, C. O.: Clinical Journal, vol. viii, p. 361.

† Nicaise, V.: Bull. Soc. Anat., 1900, p. 146.

‡ Voelcker, A. F.: Trans. Path. Soc., vol. xlvii, p. 43.

§ Thomson, H. C.: Practitioner, Oct., 1899, p. 411.

‖ Sharkey, S. J.: Trans. Path. Soc., vol. xxxv, p. 374.

** Wilks: Pathological Anatomy, p. 474.

Pressure on the intra-hepatic bile-ducts is common and results in local bile-staining of the liver tissue.

In rare instances malignant disease in the liver, after eating its way into the larger bile-ducts, may grow along the lumen of the duct without infiltrating the wall of the tube. This process is like the downward projection of a renal growth into the ureter. Cases of prolongation of malignant disease of the liver along the lumen of the bile-ducts have been described by Fauvel, Durand-Fardel,* Gilbert and Claude.†

Effects of Secondary Growths.—Secondary growths on the surface of the liver frequently set up attacks of perihepatitis and so give rise to a good deal of pain. It is very rare for a secondary growth on the surface of the liver to grow directly into the abdominal wall; this is probably prevented by the respiratory movements. It does, however, sometimes occur, and the diaphragm or anterior abdominal wall may be so firmly united by the growth to the liver that after death they can be separated only by the knife. A growth on the anterior surface of the liver may infect the opposed surface of peritoneum on the abdominal wall without any adhesions between the two, the growth being implanted by contact.

Histology.

Structurally the secondary nodules resemble the primary; but, being more rapid in their growth, are softer and more liable to break down. When secondary to carcinoma of the stomach, the hepatic growths may be either columnar-celled or spheroidal-celled; when the colon is affected, the hepatic growths are columnar-celled; in both these instances, however, the secondary tumors may differ somewhat from the primary, the cells showing a transition from the columnar to the spheroidal type. When secondary to carcinoma of the breast, the growth is spheroidal-celled; and when a primary growth in the lower part of the œsophagus infects the liver, the structure of the secondary nodules is that of a squamous-celled carcinoma. But here again from more rapid growth the cells may be spheroidal rather than squamous.

Secondary sarcoma is very often alveolar in its arrangement; this depends on the growth starting from emboli inside the small vessels of the liver.

In some cases of secondary carcinoma the cells of the liver, which are atrophied and compressed by the columns of invading cells, show very considerable pigmentation. This may be due to retained bile-pigment. In cases where the liver is independently pigmented, as in malaria or in hæmochromatosis, a secondary growth in the liver is not pigmented.

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* Fauvel, Durand-Fardel: Quoted by Devic et Gallavardin, Rev. de Méd., July, 1901, p. 570.

† Gilbert and Claude: Archiv. général. de Méd., t. clxxv, 1895, p. 513.

A man aged forty-six died under my care with a primary endotheliomatous growth in the spine. The liver was of a deep brick-red colour and had a number of minute white nodules in it, which are shown in the accompanying photomicrograph to be quite free from growth.

In some instances of secondary carcinoma there is proliferation of the liver cells in parts remote from the growth, which may be regarded as an attempt to replace the destroyed liver substance—a compensatory hyperplasia.

In a case of secondary sarcoma Cornil* observed proliferation of the hepatic cells and the formation of pseudobile canaliculi at a short distance from the growth.

Brault† has noticed that in some instances where the cells of the secondary growths contain glycogen the hepatic cells contain none.

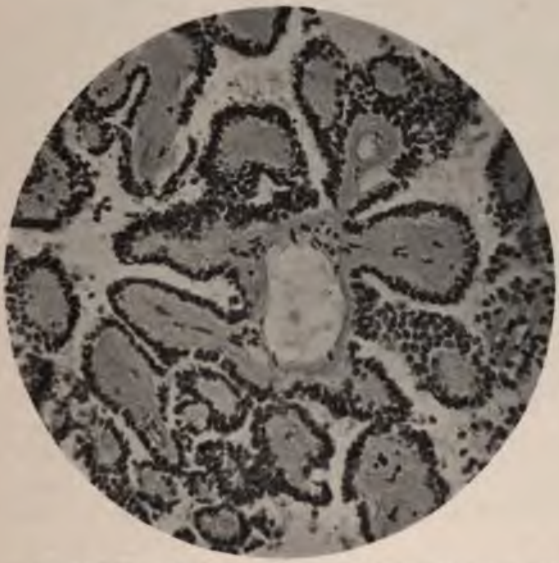

FIG. 66.—PHOTOMICROGRAPH OF A SECONDARY VILLOUS CARCINOMA OF THE LIVER. THE PRIMARY GROWTH WAS IN THE KIDNEY. (*Vide* case on p. 521. Photographed by Dr. H. Spitta.)

A certain amount of local fibrosis is often seen around carcinomatous nodules in the liver, which may be regarded as an attempt on the part of the organ to limit the extension of the growth. When this change is more general and there is obstinate jaundice, the fibrosis has been thought to be due to biliary obstruction set up by the tumor.‡

Condition of the Remainder of the Liver.—From pressure on the bile-ducts the whole or parts of the liver may be bile-stained. The occurrence of local areas of chronic venous engorgement from pressure on branches of the hepatic veins has just been referred to. In some instances the engorgement is so extreme that extravasation occurs in the immediate neighbourhood of nodules of growth and produces an appearance of a hæmorrhagic infarct. Infarctions, both hæmorrhagic and anæmic, have been met with in the liver, as a result of venous obstruction due to pressure, exerted by nodules of growths, on the portal or hepatic veins. (*Vide* p. 105.)

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* Cornil: Bull. Soc. Anat. Paris, 1902, p. 195.

† Brault: Archiv. de Méd. Expériment. et d'Anat. path., t. xiv, p. 467, 1902.

‡ Gilbert and Claude: Archiv. général. de Médecine, 1895, t. clxxv, p. 513.

Secondary malignant growths are very rare in cirrhotic livers; they occur, of course, in the special form of primary carcinoma with cirrhosis.

Hale White* mentions a case of a man with sarcoma of many bones with a growth in the liver which was hard and cirrhosed. Poulain† met with a secondary nodule of growth in a cirrhotic liver; the primary growth was a columnar-celled carcinoma of the stomach. Achard and Laubry ‡ described secondary growths in a large cirrhotic liver, the primary growth being in the colon.

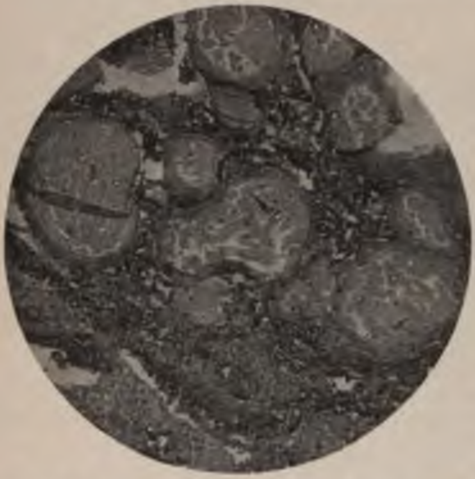

FIG. 67.—PHOTOMICROGRAPH OF LIVER WITH SECONDARY ENDOTHELIOMATOUS GROWTHS.

The liver was deeply pigmented from hæmochromatosis; the small nodules of growth were entirely free from pigment. (S. G. Penny, Esq.)

It is not very common to find cirrhosis of the liver in patients with intra-abdominal malignant disease; this is, of course, the main reason for the rarity of secondary growths in cirrhotic livers. It is conceivable that portal obstruction interferes with the passage of emboli of infecting cells from the colon and stomach, and that the cirrhotic liver is not a good soil for their development.

When, as not uncommonly happens, secondary growths occur in tight-laced livers, the constriction lobe attached to the right lobe may be quite free from growth, suggesting that its somewhat isolated position has prevented the advent of emboli of infecting cells by the blood-stream. On the other hand, secondary growth may be almost confined to the constriction lobe, as if its diminished resistance was specially favourable to the development of any embolic masses of new-growth which gain access to it. Examples of these two different events are given in the section on the tight-laced liver (p. 9).

As a coincidence secondary nodules of new-growth may develop in a liver which is already affected by hydatid disease. I have met with one such case (*vide* p. 395), and Dr. R. N. Salaman has shown me two specimens in which secondary nodules of carcinoma happened to be in actual contact with old hydatid cysts.

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* Hale White: Allbutt's System, vol. iv, p. 208.
† Poulain: Bull. Soc. Anat. Paris, Dec., 1899, p. 1089.
‡ Achard et Laubry: Soc. Méd. des Hôp., April 25, 1902, p. 335.

Secondary growths may arise in a syphilitic liver, and even in one containing gummata, but it is a rare coincidence.

A man aged forty who died with carcinoma of the colon had gummata in one testis and much scarring of the liver, which contained numerous gummata and nodules of new-growth. The man was under Dr. Cavafy in St. George's Hospital in 1891. I did the postmortem and microscopically determined that there were both gummata and new-growths in the liver.

Tubercles and secondary growths may exist in the same liver. There is no antagonism between the two processes, as was formerly thought.

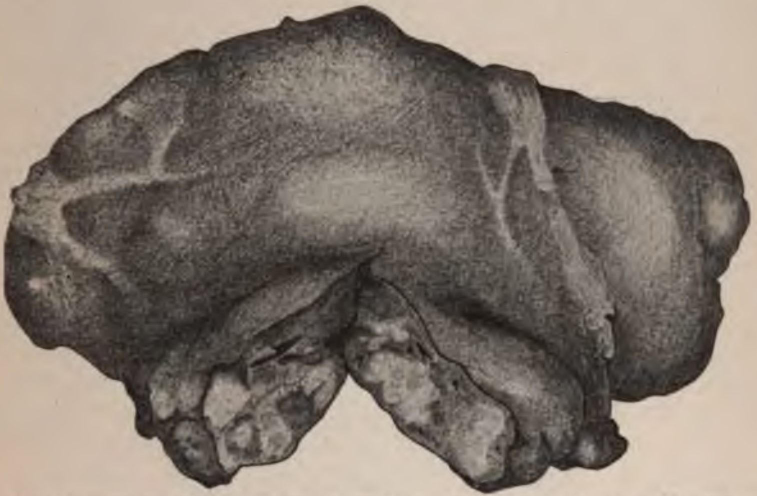

FIG. 68.—DRAWING OF A LIVER SHOWING THE CONSTRICTION LOBE DIVIDED AND ITS HALVES SEPARATED SO AS TO DISPLAY LARGE SECONDARY CARCINOMATOUS GROWTHS IN ITS SUBSTANCE.

There were in addition only two small white nodules in the right lobe of the liver. The primary growth was carcinoma of the breast. (Drawn by L. Jones, Esq., M.B., F.R.C.S.)

Dalton* briefly records a case of secondary columnar-celled carcinoma in the liver with miliary tubercles in the immediate neighbourhood. The primary growth was in the sigmoid flexure.

The existence of two different kinds of secondary growths in the same liver must be almost a unique experience.

Simon† records the case of a woman who died, two years after removal of her right eye, with widespread melanotic sarcoma. The liver was greatly enlarged with melanotic sarcoma and contained a white nodule which microscopically had the structure of columnar-celled carcinoma. Unfortunately the stomach and intestines were not examined at the autopsy, so the site of the primary growth was not discovered.

Methods of Metastasis.—The dissemination of secondary growths is due to embolism of the intra-hepatic blood-vessels. In most cases, since the primary growth is within the territory drained by the portal vein, the emboli of carcinomatous cells travel up that vessel. When the primary growth is elsewhere, as in the eye or mamma, the emboli are distributed by the hepatic artery. The dissemination of secondary growths in the liver, contrary to what is the rule in the spread of carcinoma elsewhere, is not dependent on the lymphatic vessels.

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* Dalton: Trans. Path. Soc., vol. xxxvi, p. 235.

† Simon: Bull. Soc. Anat. Paris, 1900, p. 213.

This depends on two factors: (i) That the liver does not receive the lymphatics of the other abdominal viscera, but sends its own out at the portal fissure; hence carcinoma would have to spread in against the direction of the flow of lymph. This does occasionally occur, it is true, but it is quite exceptional. In carcinoma of the stomach growth can sometimes be seen tracking into the portal fissure. Colloid cancer of the peritoneum may pass into the subserous lymphatics of the capsule and invade the liver. (ii) That the primary carcinomatous growths in the alimentary canal frequently invade the radicles of the portal vein. When this has occurred, emboli readily pass up to the liver, inasmuch as there are no valves in the portal vein.

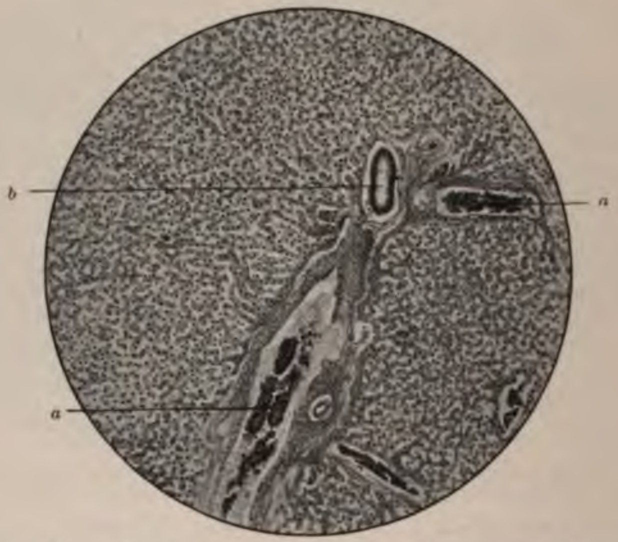

FIG. 69.—SHOWS MINUTE EMBOLI IN THE INTRA-HEPATIC BRANCHES OF THE PORTAL VEIN (*a*). A small bile-duct is represented at *b*. From a case of secondary carcinoma of the liver. The primary growth was in the stomach. × 50.

Secondary Growths due to Retrograde Embolism.—In rare instances a carcinomatous or sarcomatous embolus, when in the right auricle or inferior vena cava close to the diaphragm, is driven, by some expiratory effort, into the hepatic veins against the stream of blood. Thus Welch* refers to Heller's cases of malignant disease of the cæcum in which a loose plug of growth was found in one hepatic vein, and to Bonome's case of cancer of the thyroid gland with metastatic growths in the liver developing from plugs in the hepatic veins. My friend Professor Adami, of Montreal, has told me of a primary growth of an accessory adrenal which extended into the inferior vena cava and right auricle, where it ended in a ball-like termination and gave rise to secondary growths, evidently by retrograde embolism, in the liver.

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* Welch: Allbutt's System of Medicine, vol. vi, p. 232.

Direct Invasion of the Liver by a Growth.—It is not very uncommon for a growth starting in the gall-bladder to infiltrate the liver by direct continuity, and in some instances the appearances have led to an erroneous diagnosis of primary malignant disease of the liver. Primary carcinoma of the extrahepatic bile-ducts may extend up into the liver.

Malignant disease of the stomach, especially at the cardiac end, may spread directly into the substance of the liver. In Fenwick's* 131 cases of gastric carcinoma this occurred in 13.7 per cent. In such cases the growth in the liver may undergo necrosis or become infected and give rise to a gangrenous abscess cavity and to a certain amount of fever. In rare instances carcinoma of the lower end of the œsophagus may extend directly into the liver. I have seen direct invasion of the liver occur in cases of primary endothelioma of the right suprarenal body.

SITUATION OF THE PRIMARY GROWTH IN SECONDARY MALIGNANT DISEASE OF THE LIVER.

The most frequent sites of the primary carcinomatous growths are in the alimentary canal, viz., stomach, colon, œsophagus, pancreas, from which small emboli of infecting cells pass along the portal vein and form carcinomatous emboli in the capillaries of the liver; thus secondary growths start, and are for a time inside the hepatic capillaries, while primary carcinoma is outside the vessels, or extra-vascular.

In 100 consecutive cases of secondary malignant disease of liver abstracted from the postmortem books of St. George's Hospital from 1892–1902 the following were the situations of the primary growths:

Carcinoma.	
Stomach	24
Colon	12
Œsophagus	10
Pancreas	8
Gall-bladder	5
Uterus	4
Mamma	3
Kidneys	3
Bile-ducts	3
Biliary papilla	1
Vermiform appendix	1
Bladder	1
Ovary	1
Generalized	1
	77

Sarcoma.	
Suprarenal bodies	5
Mediastinum	4
Melanotic	3
Generalized	3
Bone	2
Lung	2
Stomach	1
Liver	1
Thyroid	1
Uterus	1
	23

The stomach is the most frequent site of the primary growth in secondary malignant disease of the liver. According to Hale White,†

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* Fenwick: Cancer and other Tumors of the Stomach, p. 55.

† Hale White: Allbutt's System of Medicine, vol. iv, p. 197.

25 per cent. of the cases of secondary malignant disease of the liver are secondary to malignant disease of the stomach; this is practically the same as my own estimate.

In malignant disease of the stomach there are secondary growths in the liver in about 35 per cent. of the cases (Fenwick*). Welch gives 30 per cent., Perry and Shaw,† 40 per cent., and Lebert, 40.9 per cent. In 47 fatal cases of gastric carcinoma tabulated by Osler and McCrae‡ the liver was affected in 23. According to Fenwick, the right lobe is involved in carcinoma of the pylorus and middle of the stomach, and the left lobe when the cardiac end is the site of carcinoma.

Carcinoma of the colon is probably, after malignant disease of the stomach, the most frequent cause of secondary growths in the liver.

In 100 cases of secondary malignant disease of the liver the colon or rectum was the site of the primary growth in 12. In 100 fatal cases of primary carcinoma of the colon examined after death I found that secondary growths occurred in the liver in 34. But in many of these the secondary nodules were quite small and could not have given rise to any clinical manifestations. Of these 100 cases, 52 were males (19 secondary growths) and 48 females (15 secondary growths).

It is a remarkable fact that secondary growths in the liver are more frequent and often more extensive when the primary growth in the colon is small than when it is large. A patient may be quite unconscious of a growth in the rectum when the liver is greatly enlarged. Hence the rectum should always be examined in suspected cases of malignant disease of the liver when the site of the primary growth is not at once clear.

The following is a typical example of extensive malignant disease of the liver following carcinoma of the sigmoid flexure:

Primary Carcinoma of the Sigmoid Flexure, Secondary Growths in the Liver, Asthenia, Slight Jaundice, and Ascites; Death in Coma.—A man aged fifty-six was admitted into St. George's Hospital on July 6, 1900, with abdominal pain, rapid emaciation, and increasing weakness. He was slightly jaundiced, had a large, knobby liver, which was hard and tender. The patient had had pain on defæcation and had passed blood by the bowel. He complained of constant perspiration. There was some œdema of the feet. His condition was very bad, and on July 13th he became comatose and died in twenty-four hours. At the autopsy there was a primary columnar-celled carcinoma in the lower part of the sigmoid flexure. The liver weighed 11 pounds and was stuffed with white, almost caseous, growths; there were no growths anywhere else. There was some ascites.

Metastatic growths in the liver are found in about half the cases of **primary carcinoma of the gall-bladder.**

In Musser's§ 100 cases the liver contained secondary nodules in 52 and was directly invaded by the growth in 2 more.

Secondary growths are frequently found in the liver in fatal cases of **carcinoma of the breast.** Thus in 423 postmortem examinations of mammary carcinoma tabulated by Gross,‖ the liver was affected in 206, or 48.6 per cent.; in 735 cases investigated by S. Paget* the liver was involved in 241, or 34 per cent. This is much lower than Gross's estimate, and is much the same as Beadles'† observation that in 100 cases of malignant disease of various parts of the body secondary growths in the liver were found in 36.

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* Fenwick: Cancer and Other Tumors of the Stomach, p. 182.

† Guy's Hosp. Reps., vol. lviii, p. 155.

‡ Osler and McCrae: Cancer of the Stomach, p. 141.

§ Musser: Boston Medical and Surgical Journ., vol. cxxi, 1889.

‖ Gross: American Journ. Med. Sciences, vol. xc, p. 235, 1888.

Carcinoma of the œsophagus is more likely to lead to secondary growths in the liver when the lower third of the gullet is the site of the growth.

In 55 cases of œsophageal carcinoma there were secondary nodules in the liver in 10 instances.‡

Secondary Sarcoma.—As has already been pointed out, secondary sarcoma is much less frequent in the liver than secondary carcinoma. (*Vide* p. 485.) Hale White found 7.35 per cent. of secondary sarcoma. My figures, which give a much higher percentage of secondary sarcoma, viz., 23, include cases of endothelioma, for example, malignant growths primary in the suprarenal glands.

Melanotic Sarcoma.—The occurrence of secondary melanotic growths in the liver is well known, and is such a striking morbid lesion that once seen—and all museums have specimens illustrating it—it is never forgotten. Since this is a condition every one is familiar with and is a matter, so to speak, of common knowledge, it might be thought that it is frequently met with in ordinary hospital work. This, however, is not the case.

In twelve years—1890-1901—there were 3806 postmortem examinations performed at St. George's Hospital, and in 3 cases there were secondary melanotic growths in the liver, or in 0.08 per cent.

The primary sites of malignant melanotic growths are chiefly those where the pigment melanin is normally present, viz., in the uveal tract and in the skin, especially in pigmented moles. It may be mentioned that melanotic cutaneous growths, though from custom usually spoken of as sarcomata, are now generally regarded as pigmented endotheliomatous growths. In rare instances a primary melanoma has been seen in the rectum or at the margin of the anus, but secondary growths in the liver are very rare in these cases.

De Buck and Vanderlinden§ describe a case with secondary growths in the liver. In neither Heaton's ‖ case nor one examined by myself were there hepatic metastases.

Recurrence in the liver usually occurs within three years of the appearance of the primary growth, and the prognosis is very bad. Occasionally long periods of immunity are met with. In one of the first published cases of secondary melanotic sarcoma there was an interval of eight or nine years between the removal of the eye and the occurrence of symptoms indicating hepatic growth.[*]

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* Paget, S.: Lancet, 1889, vol. i, p. 571.

† Beadles, C. F.: Trans. Path. Soc., vol. xlvii, p. 77.

‡ Allbutt's System of Medicine, vol. iii, p. 374.

§ De Buck and Vanderlinden: Belgique Méd., Nov. 9, 1899.

‖ Heaton: Trans. Path. Soc., vol. xlv, p. 85.

Fisher and Box[†] reported to the Ophthalmological Society a case of primary pigmented tumor of the eye removed fourteen years before death from generalised pigmented carcinoma affecting the liver (which weighed 21 pounds 6 ounces), lungs, bones of the skull, and heart. The pigmented tumor in the eye appears to have been a sarcoma; so the patient was the subject of two independent outbreaks of malignant disease. This case is referred to elsewhere (p. 479) as a possible example of primary melanotic carcinoma of the liver.

Lawbaugh[‡] has briefly recorded a case where seventeen years elapsed between enucleation of the eye for a melanotic sarcoma and death from the same growth in the liver. The most extraordinary case is one in which there were thirty-two years between the removal of the eye for melanotic sarcoma and death from the same disease in the liver. Wilder,[§] who mentions this case, saw the liver in Kundrat's laboratory at Vienna.

Very occasionally the liver may be widely infiltrated with secondary melanotic sarcoma, while the primary growth is very small and may escape notice.

In the London Hospital Museum[||] there is a liver infiltrated with melanotic sarcoma and weighing 16 pounds; the primary growth in the eye was only discovered at the autopsy.

Dr. Newton Pitt has kindly given me notes of a similar case. A man aged twenty-nine had cutaneous tumors, one of which was excised and found to be an alveolar melanotic sarcoma, and enlargement of the liver. Ophthalmoscopic examination of the eyes was negative. There was no melanin in the urine. At the postmortem there was extremely widespread generalisation of the growth; the liver weighed 16 pounds. There was a small growth in the outer edge of the uveal tract in the right eye.

Lawford and Collins and C. D. Marshall have collected statistics as to the results of melanotic sarcoma of the uveal tract. The former observers found that in 26 cases that were known to have died there was evidence that the liver was affected in 16.

In age-incidence malignant melanotic growths resemble carcinoma and rarely occur in early life.

In 103 cases of sarcoma of the uveal tract, all of which, except one, where no note was made, being more or less melanotic, collected by Lawford and Collins,[**] the average age was 48.4 years, the extremes of age being 15 years and 84 years. In 35 cases of secondary melanotic growths in the liver which I have collected, the average age almost exactly corresponds to this, being 48.7 years, or 46.7 years for the males and 53.3 for the females, the extremes being 27 years and 75 years.

Of Lawford's and Collins' 103 cases, 59 were males and 44 were females; in my 35 collected cases where the sex was stated 25 were males and 10 were females; this shows a much more marked preference for males than in the series of primary growths of the uveal tract. The right eye was affected 41 times and the left 60 times in Lawford's and Collins' cases, while in the cases I have collected of hepatic growths the right eye was rather more frequently the primary seat of growth, but the numbers are small.

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[*] Murchison: Trans. Path. Soc., vol. xxiv, p. 123.

[†] Fisher and Box: Brit. Med. Journ., 1900, vol. i, p. 639.

[‡] Lawbaugh: Journ. of the American Med. Assoc., Nov. 24, 1900, p. 1363.

[§] Wilder: Ibid.

[||] *Vide* London Hospital Gaz., Clinical Supplement, June, 1900.

[**] Royal London Ophthalmic Hospital Reports, vol. xiii, p. 104.

Metastatic melanotic tumors of the liver are more often secondary to a primary growth in the uveal tract than in the skin. Thus, in 37 cases of melanotic sarcoma in the liver the primary growth was 24 times in the eye and 13 times in the skin. This is partly due to melanotic sarcoma being commoner in the uveal tract than in the skin. Examination of the recorded cases shows that the growths in the liver following cutaneous melanosis are not so big or so striking as those following melanotic sarcoma of the uveal tract. Primary cutaneous melanotic growths may, indeed, give rise to very widespread secondary growths in the viscera, the liver being one of the few organs not affected. In most of the cases I have collected where the liver contained secondary growths following cutaneous melanosis, the organ was little above the ordinary size, though in two cases it weighed over 7 pounds, while, on the other hand, some of the largest livers recorded have been due to melanotic sarcoma originating in the eye. Thus Litten* has described a case where the liver weighed 27 pounds, Sayre† one of 23 pounds, and Hamburger‡ one of 22 pounds. In two cases that I have examined myself the weight was in both within a few ounces of 16 pounds. The average weight of the liver in 22 cases of melanotic growth secondary to a growth in the uveal tract was 13 pounds 3 ounces.

In a case§ where the growth began in the left toe there were numerous growths in the skin elsewhere, the lungs, kidneys, and brain, but the liver and spleen were quite free.

The two following cases illustrate the difference in the tendency to metastasis in the liver exhibited by melanotic sarcoma starting in the skin, on the one hand, and when it is primary in the eye, on the other hand.

Primary Growth in the Skin of the Big Toe; Widespread Metastasis.—A man aged sixty-four years had had his foot removed for a melanotic sarcoma starting in the big toe after an injury. The growth recurred in the stump, and at the autopsy, which I performed, there were metastases in the lungs, brain, left kidney, pancreas, abdominal glands, and liver. The liver contained numerous isolated growths, but weighed only 52 ounces. The growth was a spindle-celled sarcoma.

Primary Growth in the Eye, Excision, Recurrence in the Liver.—A man aged fifty-nine years was admitted under my care with the history that his right eye had been removed two years previously for a melanotic sarcoma. The liver was enormously enlarged and knobby, but there was no ascites. He had melanuria. The legs were œdematous. At the autopsy there were a few small secondary growths on the diaphragm, in the mucous membrane of the intestine, and in one adrenal body. The liver was enormously enlarged, weighing 15 pounds 12 ounces, and was extensively occupied by growths of a spindle-celled melanotic sarcoma.

The liver is a very favourite site for secondary infiltration in melanotic sarcoma of the uveal tract. In a few cases it is found to co-exist with an intra-ocular growth, but it usually occurs within three years after removal of the eye and generally without there being any local recurrence in the optic nerve or orbit. It would thus appear that the infective cells of the growth must remain latent in the liver for some time. The liver may, indeed, be the only organ in the body affected, while in other instances almost every viscus and tissue shows metastases. It is remarkable that the cells of melanotic sarcoma being, as they usually are, larger than the cells of the other sarcomata which are stopped by the lungs, manage to pass through the pulmonary capillaries and to infect the liver.

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* Deutsche med. Wochen., Bd. xv, S. 41, 1889.

† Transactions of the New York Pathological Society, 1879, vol. iii, p. 42.

‡ Johns Hopkins Hospital Bull., March, 1898.

§ Levi: Bull. Soc. Anat. Paris, 1899, p. 709.

The liver evidently offers the most favourable situation for the growth of melanotic sarcoma. But though it may be the only organ affected, as a rule secondary growths are very widely disseminated throughout the body. The growths in the liver almost always progress very rapidly, but in Litten's* case there was evidence of a tumor of some kind in the liver for the exceptionally long period of four years.

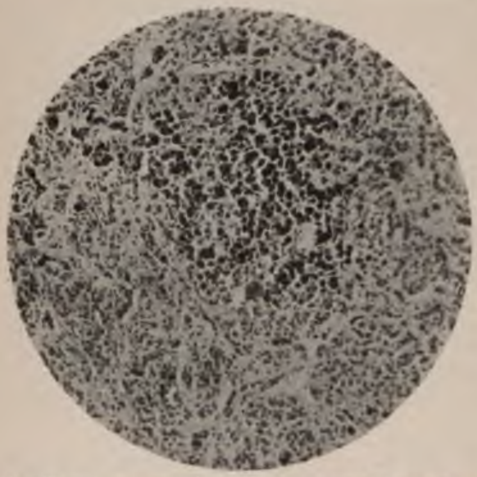

FIG. 70.—SECONDARY INFILTRATION OF THE LIVER WITH A MELANOTIC SARCOMA.

The cells are chiefly round-cells, and vary very considerably in the amount of melanin they contain. The arrangement is more or less alveolar. The primary growth was in the uveal tract. (Photomicrograph by S. G. Penny, Esq.)

The liver may be either nodular, from the presence of discrete growths, or there may be diffuse infiltration, so that the organ, though enlarged, is not altered in shape. When infiltrated with melanotic growth, the liver substance presents a variegated appearance like that of granite. In exceptional cases the liver is so extensively infiltrated that it looks as if it had been soaked in tar. Not uncommonly the liver shows nodules in some parts and diffuse infiltration in others. As a rare event a pedunculated growth may be found attached to the liver. I have seen this once. Sometimes parts of the growths are free from pigment and appear white; in other cases the pigment is sparse and the tumors, to the naked eye, appear of a mottled grey or greenish colour.

Histologically, secondary melanotic growths in the liver may be sarcomatous or endotheliomatous; when sarcomatous, they may be spindle-celled, oval or oat-shaped, or round-celled. The cells start as emboli inside the hepatic capillaries, and hence the growth frequently has a more or less alveolar appearance.

Malignant Disease Primary in the Suprarenal Glands.—In 26 cases of primary malignant disease (carcinoma, endothelioma, or sarcoma) of the adrenal bodies collected by Marks and myself* the liver was the organ most frequently affected by secondary growths, viz., in 14, and was, in addition, invaded by direct continuity in 3. In 46 cases of sarcoma of the suprarenal glands collected by Pepper† there were metastases in the liver in 14. A suprarenal growth may extend into the inferior vena cava and give rise to retrograde embolism in the hepatic veins and so to secondary growths, as in Adami's case (p. 495).

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* Litten: Deutsch. med. Woch., 1889, S. 41.

In generalised sarcoma the liver often shows discrete nodules of growth. The portal spaces may be infiltrated with green growth in the interesting though very rare disease, chloroma, which has been regarded in the past as a form of round-celled sarcoma, but is probably lymphatic leukæmia. Trevithick‡ has recently reported a case of this kind.

An exceptional origin for secondary growths in the liver is so interesting that a brief reference may be made to it. Embryomata and teratomata in the abdominal cavity may take on malignant growth and infect the liver.

Out of 10 cases of malignant teratomata collected by Montgomery,§ four led to secondary growths in the liver. Hulke ‖ described a secondary dermoid growth on the surface of the liver following rupture of an ovarian embryoma (dermoid). The same kind of generalisation, or rather implantation, took place in a case briefly described by Latham.** Abdominal dermoids (embryomata) are practically teratomata, as they are not composed of skin alone, but of tissues derived from all three layers of the embryo, and are really, as Wilms †† showed, complex tumors.

CLINICAL FEATURES OF MALIGNANT DISEASE OF THE LIVER.

It will be most convenient to describe the signs and symptoms of both primary and secondary malignant disease of the liver together, since the two conditions are so frequently indistinguishable, and to note the points of difference between them in a special section (*vide* p. 520).

The latency of malignant disease of the liver is dealt with on page 514, under the heading of Diagnosis.

PHYSICAL SIGNS.

The facial aspect of a patient with advanced malignant disease of the liver is that of a grave and wasting illness. The eyes are usually sunken, and the skin dirty, sallow, or showing varying degrees of jaundice. But in the earlier stages, even when nodular enlargement of the liver can be felt, there may be little to note in the patient's aspect except some anæmia, and it cannot be maintained that the facial aspect is characteristic at this early stage. Steady loss of flesh and weight is very commonly met with in malignant disease of the liver. The subcutaneous fat is absorbed, and as a result the cheeks and temples fall in and give rise to a hollow and haggard appearance to the patient. Absorption of fat helps to render the skin inelastic.

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* Rolleston and Marks: American Journ. Med. Sciences, vol. cxvi, p. 390.

† Pepper: Ibid., vol. cxxi, p. 287.

‡ Trevithick: Lancet, 1903, vol. ii, p. 158.

§ Montgomery: Journ. Experiment. Med., May, 1898.

‖ Hulke: Trans. Path. Soc., vol. xxiv, p. 157.

** Latham, A.: Trans. Path. Soc., vol. l, p. 232.

†† Wilms: Deutsch. Arch. f. klin. Med., Bd. lv, S. 289.

It has been noticed that during the emaciation an associated fatty tumor has greatly diminished in size from absorption of its fat. (Bell.*)

In very rare instances the patients actually gain in weight as the liver increases in size.

In a case recorded by Delépine † a man with primary melanotic sarcoma gained 3 pounds in weight during the last three months of life. A boy, aged fifteen years, who died with primary carcinoma of the liver, gained 19¾ pounds before his death; this was due to the enormous size of the liver, which weighed nearly 16 pounds, or two-fifteenths of the total body weight, and also to the presence of ascites. (Acland and Dudgeon.‡)

The gain in weight of the individual as a whole depends on the increase from the tumor growth more than counterbalancing the loss due to general emaciation. The same phenomenon is sometimes seen in rapidly growing renal sarcomata in infants. Some increase in weight and improvement in general nutrition may follow on careful feeding, especially in the early stages of malignant disease of the liver.

Progressive emaciation is more marked in cases of secondary malignant disease of the liver, for here there is in addition the effect of the primary growth, often in the stomach or colon, which has already, and perhaps for some considerable time, interfered with digestion and assimilation of food. In such cases nutrition may be so impaired that bed-sores develop; their occurrence is probably favoured by the fact that the patient generally lies in one position—on the back.

Exceptionally, however, death may occur from secondary malignant disease of the liver when the patient is well nourished or even fat.

A man aged sixty-three years, a patient in St. George's Hospital, had enlargement of the liver and ascites. He had never had any hæmatemesis and was not jaundiced. He was thought to have cirrhosis. At the autopsy, the abdominal walls, mesentery, etc., contained much fat. There was a primary carcinoma of the hepatic flexure, and the liver, which weighed 10½ pounds, was full of secondary growths.

In primary malignant disease the progress of the disease is so rapid, death often following even within three months of the first symptoms, that there may not be time for emaciation and there may be plenty of subcutaneous fat.

In a very rapid case which I examined postmortem some years ago the man —who was, by the way, sent into the hospital for intestinal obstruction—was very fat. An enormously fat woman aged forty, weighing over 20 stone, died with multiple growths in the liver, which weighed 10 pounds 11 ounces. Except for a few minute nodules in the spleen, no other growth could be found elsewhere in the body. It was apparently a case of multiple primary carcinoma of the liver. Microscopically the growth was a rapidly growing carcinoma composed of cells showing transitional forms from columnar to spheroidal type.

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* Bell: Brit. Med. Journ., 1902, vol. i, p. 1588.

† Delépine, S.: Trans. Path. Soc., vol. xlii, p. 170.

‡ Acland and Dudgeon: Lancet, 1902, vol. ii, p. 1310.

Cachexia is important in differentiating malignant from other enlargements of the liver, such as deeply seated hydatid cysts, hypertrophic biliary cirrhosis, and from some cases of nutmeg liver. The *progressive* character of the cachexia is of especial importance. The causation of cachexia is probably to be found in an auto-intoxication emanating from the rapidly proliferating epithelial growths. As is well known, the cells of many normal glands, such as the pancreas, thyroid, suprarenal, provide an internal secretion which passes directly into the lymphatics or veins, and helps to keep up the condition of equilibrium we know as health. When epithelial cells run riot and form *atypical* growths, or what might be called abnormal glands, it is not unreasonable to believe that they may produce a morbid internal secretion which, when absorbed, poisons the body generally, and gives rise to the cachexia of malignant disease. In support of this view it is noticeable that innocent tumors composed of normal tissues do not, however large they may be, give rise to cachexia, unless they mechanically interfere with absorption and nutrition. There are other ways in which poisonous substances can be supplied by malignant growths. As the result of necrosis and disintegration of growths, toxic bodies are probably produced which, when absorbed, will tend to produce toxæmia and cachexia.

Fever.—It is generally believed that malignant disease of the liver is not accompanied by fever or only by transient elevations of temperature due to independent causes. This, however, is very far from being a hard-and-fast rule. Eggel * estimated that fever was present in 14 per cent. of the 147 cases of primary carcinoma of the liver which he collected. It is important to recognise that fever may be present in malignant disease of the liver, whether primary or secondary, and that the existence of a raised temperature does not necessarily exclude new-growth in favour of some form of hepatic suppuration. In malignant disease the temperature, if raised, is usually irregular and not very high, but if complicated by suppuration, it may closely imitate hepatic abscess.

The raised temperature may be due to the rapid growth and multiplication of cells inside the liver; cases occur in which no other cause is forthcoming; this may be seen in primary malignant disease of the liver. The liver forms a very suitable soil for rapid tumor growth and hence fever is more often seen in malignant disease of the liver than of other organs.

Fever is, moreover, not very rare in malignant disease elsewhere in the body; as pointed out by Butlin and Colby, fever is not very uncommon in cases of sarcoma of the femur and tibia.

In secondary malignant disease of the liver fever may be independent of the rapid cellular proliferation and destruction in that organ, and may be due to toxic or septic absorption from the ulcerated surface of the primary growth in the stomach, colon, or elsewhere. Again, the necrotic growths may become infected with micro-organisms either from the alimentary canal or from the blood-stream, and from these secondary infections fever and rigors may result. Suppuration is occasionally found

* Eggel: Ziegler's Beiträge Bd. xxx, 1901.

in association with secondary growths in the liver. In some instances a primary growth in the stomach may directly invade the liver and carry infection into that organ.

A woman aged fifty-four had a primary spheroidal-celled carcinoma of the cardiac end of the stomach which perforated directly into the under surface of the liver and produced a large abscess in close contact with numerous secondary nodules in the liver. The hepatic abscess leaked into the peritoneal cavity and set up fatal peritonitis.

Suppurative cholangitis may develop in the course of malignant disease of the liver when the ducts are dilated from obstruction.; this is more likely to occur in secondary malignant disease of the liver, since obstruction to the ducts is comparatively infrequent in primary growths of the liver substance.

Osler * refers to a case of cancer of the liver where intermittent fever and rigors were so marked that the question of abscess was raised during life. After death, in addition to secondary growths, there were several abscesses caused by the growths compressing the bile-ducts.

A good example was seen in a woman aged forty-four who had jaundice due to growths in the portal fissure, secondary to carcinoma of the splenic flexure of the colon, compressing the hepatic ducts. The intra-hepatic bile-ducts showed suppuration. There was high fever in this case, which was under the care of my colleague, Sir Isambard Owen.

Primary carcinoma of the second part of the duodenum involving the biliary papilla (perivaterian duodenal carcinoma) is especially prone to set up suppurative cholangitis; usually it kills the patient in this way before there has been time for secondary growths to occur in the liver, but secondary growths may be found in association with suppurative cholangitis.

A man aged fifty-two was under the care of my colleague, Sir Isambard Owen, with jaundice, rigors, and a lump in the prostate. At the necropsy there was a primary columnar-celled carcinoma of the biliary papilla, secondary growths in the liver, suppurative cholangitis, and empyema of the gall-bladder, and pyæmic abscesses in the prostate and kidneys.

A resemblance between malignant disease and cirrhosis of the liver may be noted in the fact that fever may occur in both, from secondary infections or from auto-intoxication. Cases of malignant disease of the liver with fever may thus simulate pylephlebitis, hepatic abscess, or possibly even typhoid fever.

The liver is enlarged, and the enlargement is progressive. When the surface of the organ is irregular, the growth is in the great majority of cases secondary; the nodules may be felt to be umbilicated or depressed in the centre, and thus can be distinguished from the hobnails of a cirrhotic liver, from which the progressive character of the enlargement further separates it.

It does, however, sometimes happen that the depression between hobnails on a cirrhotic liver conveys the impression of umbilication, while umbilication cannot always be felt over secondary hepatic growths. In cirrhosis the enlargement is more uniform than in malignant disease which chiefly affects the right lobe.

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* Osler: Johns Hopkins Hospital Reports, vol. ii, No. 1.

In primary malignant disease of the liver there is usually a uniform, firm, and hard tumor in the position of the right lobe of the liver. Occasionally there are, in addition, nodules of secondary growth elsewhere on the surface of the liver. This condition cannot be distinguished from secondary malignant disease in which the primary growth is latent. Occasionally the growth is so soft that it fluctuates and imitates an abscess. (*Vide* p. 517.) In rare cases it may pulsate, either because the growth is a hæmorrhagic sarcoma or from transmitted pulsation.

Sir T. Lauder Brunton * met with a case of malignant disease of the left lobe of the liver with pulsation and a bruit over the tumor which imitated an abdominal aneurysm.

A mass of new-growth may be found at the umbilicus in association with secondary malignant disease of the liver. Small outlying secondary growths may also form in the falciform ligament of the liver, and be felt during life near the linea alba; their presence greatly assists in forming a diagnosis of malignant disease. They may, however, be closely simulated by small islands of fat left intact when emaciation is proceeding rapidly.

In a case of secondary malignant disease of the liver in which small masses were felt during life in the line of the falciform ligament I could not find postmortem the growths which I thought I had felt during life, and which had assisted in the diagnosis.

Nodules of new-growth on the surface of the liver may, of course, be closely simulated by perihepatitic adhesions or by irregularities due to gummata and syphilitic cicatrices.

A venous hum or murmur is occasionally heard over the liver. It may be due to pressure, exerted by nodules of growth or enlarged glands, on the portal vein, or possibly to constriction of the inferior vena cava where it is in contact with the liver. *Friction* from perihepatitis, set up by growths involving the capsule, may be detected in some instances and is usually accompanied by pain and tenderness on pressure. It is commoner in secondary than in primary growths of the liver, not only because secondary growths are met with in such an overwhelming proportion, but because they are more likely to involve the capsule than primary growths.

Hæmorrhages into the skin, mucous membranes, and other parts of the body may occur in association with jaundice and cholæmia. They may also be met with when there is little or no jaundice, though the liver is extensively infiltrated by growth or when rapidly destructive changes in the liver cells, allied to those of icterus gravis, are in progress. As the result of failure in the protective or antitoxic function of the liver cells, poisons absorbed from the intestinal tract pass into the general circulation and give rise to the manifestations of cholæmia. The presence of bile in the circulation is quite subordinate in importance to these toxic substances.

Jaundice and **ascites** are not essential, but rather accidental, symptoms of malignant disease of the liver. Their occurrence may be due to a piece of the growth pressing on the portal vein and bile-duct, or on their main branches; a secondary growth in the glands in the portal fissure may thus give rise to both.

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* T. Lauder Brunton: Trans. Med. Soc. London, vol. xix, 1896.

One or both of them may appear almost at any period of the disease. They are not evidences of the extent or severity of the disease, but only of its situation. They both occur in about 50 per cent. of the cases.

Jaundice, if marked, is a severe complication, and by giving rise to cholæmia may accelerate the necessarily fatal issue of the case. In a collection of cases of primary malignant disease of the liver Hale White * found that jaundice when present was comparatively slight and not of the marked character and prolonged duration sometimes met with in secondary malignant disease of the organ. Jaundice is sometimes dependent on the associated catarrh of the bile-ducts and not necessarily on mechanical pressure, and may then be relieved by treatment. (Mayo Robson.†) During life, however, jaundice in malignant disease is generally explained by mechanical pressure; though if it disappeared, catarrhal swelling of the duct might suggest itself. The onset of jaundice in malignant disease may be sudden and accompanied by sickness and vomiting, so as to simulate catarrhal jaundice very closely, but instead of disappearing, it persists and becomes deeper.

In secondary malignant disease of the liver jaundice is rather more likely to supervene and to occur early when the primary growth is situated near the bile-ducts, as, for example, at the pylorus or in the gall-bladder. Primary growth in these positions is prone to spread directly to the portal fissure and to produce obstructive jaundice, while multiple embolic nodules of growth scattered broadcast over the periphery of the liver have much less tendency to induce biliary obstruction. The following case illustrates this point:

A man aged thirty-four years became jaundiced a few weeks before his death from primary spheroidal-celled carcinoma near the pylorus. The lesser omentum was ¾ inch thick, being infiltrated with growth which surrounded and compressed the common bile-duct. Microscopically the bile-duct was much infiltrated with growth, the infiltration extending up to the neck of the gall-bladder and into the portal fissure. The gall-bladder and intra-hepatic bile-ducts were distended, but the extra-hepatic ducts were all compressed. The liver weighed 66 ounces and had a green, nutmeggy appearance; there were small masses of growth in the intra-hepatic branches of the portal vein. This patient was under the care of Dr. Penrose in St. George's Hospital.

Obstruction to one of the intra-hepatic bile-ducts, provided it be fairly large, may give rise to jaundice; in such a case the other bile-ducts convey bile into the intestine and the fæces are not clay-coloured. At the autopsy of such cases pressure on the gall-bladder will cause bile to flow into the duodenum. This was shown in the following case:

A man aged fifty-five years, a barman, was admitted to St. George's Hospital under my colleague, Dr. Penrose, with a large liver and distinctly palpable glands above the right clavicle. The liver was manifestly knobby, but no umbilication could be made out. The urine contained much urobilin; the fæces contained

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[illegible] White: Guy's Hospital Reports, 1890, p. 59.

[illegible] Robson: Brit. Med. Journ., 1897, vol. i, p. 641.

bile, and jaundice of no great intensity finally developed. Except for some difficulty in swallowing, there was nothing to suggest the site of the primary growth. At the autopsy the liver weighed 14 pounds, and contained numerous secondary growths, some of which were umbilicated. Pressure on the gall-bladder brought bile out of the duodenal papilla. There were numerous growths in the liver near the portal fissure, which compressed some of the bile-ducts. No calculi; no cirrhosis of the liver, which was somewhat nutmeggy. Spleen showed venous engorgement. There was a primary spheroidal-celled carcinoma in the middle third of the œsophagus, and a secondary growth, probably due to implantation, much resembling to the naked eye another primary neoplasm, at the cardiac end of the œsophagus. There were a few ounces only of ascitic fluid.

On the other hand, it should be noted that experimental ligature of the left hepatic duct in cats performed by V. Harley and Barratt * did not give rise to jaundice. Possibly this was due to some collateral biliary anastomoses between the right and left lobes of the liver.

An interesting but extremely rare, cause for jaundice is extension of malignant disease along the lumen of the bile-ducts in an analogous manner to the prolongation of a renal growth down the ureter.

Gilbert and Claude † have recorded primary carcinoma of the liver in a girl aged twenty-two, in whom attacks of biliary colic and obstinate jaundice were due to a process of the growth extending along and blocking up the common bile-duct. The growth did not infiltrate the walls, but grew in a polypoid form along the lumen of the duct.

When jaundice is absent, the skin is usually anæmic, sallow, and sometimes dirty-looking; slight pigmentation, as in other forms of abdominal disease, is sometimes seen.

Legg ‡ figures marked pigmentation suggesting argyria in a man with melanotic growths in a liver weighing 5700 grammes (178 ounces) who also had melanuria. Williamson § lays stress on small black patches appearing on the skin as diagnostic of internal melanotic growth; he also mentions pigmented nodules which would naturally suggest melanotic sarcoma.

Ascites.—When the liver is extensively infiltrated with new-growth its capillaries become obstructed over a correspondingly wide area, either by pressure from without, as in primary carcinoma, or from the presence of growth inside their lumen, as in secondary growth, and especially in one form of primary angiosarcoma (endothelioma).

Hektoen and Herrick ‖ have drawn special attention to embolic blocking of the capillaries in secondary melanotic sarcoma of the liver.

The obstructed portal circulation thus resembles that in portal cirrhosis, and an attempt at compensation by dilatation of the veins at the lower end of the œsophagus may be found in some cases.

In a case under my care of secondary melanotic sarcoma of the liver, which weighed 16 pounds, there were markedly varicose veins at the lower end of the œsophagus. Frerichs ** records a similar case.

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* Brit. Med. Journal, 1898, vol. ii, p. 1743.

† Gilbert and Claude: Archiv. gén. de Médécine, 1895, t. clxxv, p. 513.

‡ Legg: Trans. Path. Soc. London, vol. xxxv, p. 367.

§ Williamson, R. T.: Lancet, Dec. 29, 1900, vol. ii, p. 1874.

‖ Hektoen and Herrick: American Journal of the Medical Sciences, vol. cxvi, p. 255, 1898.

** Frerichs: Diseases of Liver, vol. ii, p. 239, New Sydenham Soc.

Portal thrombosis due to an extension of the growth from the intrahepatic branches into the trunk of the portal vein may also account for ascites in malignant disease of the liver, but it is usually due to concomitant malignant disease of the peritoneum or to local inflammation of the capsule of the liver set up by an underlying growth.

The ascitic fluid is usually serous and clear, like that in cirrhosis or in simple chronic peritonitis, but is bile-stained when there is jaundice. The effusion may be blood-stained from extravasation of blood into the growths, especially when they are necrotic and have ruptured into the general peritoneal cavity. In some cases, especially in sarcoma, the loss of blood, due to extravasation into the growths, may be so excessive as to give rise to faintness and collapse, while at the same time there is marked increase in the size of the hepatic tumor, which may even fluctuate and imitate very closely hepatic abscess.

Cases of this kind have been recorded by Byrom Bramwell,[*] Hawthorne,[†] and others.

It has been stated that ascites is rare or even that it does not occur in melanotic sarcoma of the liver, but this is not borne out by the cases I have collected, for it was stated to be present in 10 of the 37 collected cases of secondary melanotic disease of the liver; and in at least three of the reputed primary melanotic growths of the liver there was ascites; in a case examined by Dr. Penrose in St. George's Hospital in 1888 there was as much as three gallons of fluid. Occasionally in these cases the ascitic fluid is of a dark colour, from the presence of melanin; more often it is like ordinary ascitic fluid.

In a woman aged thirty-three who died with melanotic sarcoma of the liver there were 100 ounces of dark fluid in the peritoneal cavity and a pint of brown fluid in each pleura. (Middlesex Hosp. Reports, 1890–91, p. 278.) In this case the colour was presumably due to the escape of melanin from the melanotic sarcoma. Wickham Legg[‡] and Senator[§] have also recorded cases of melanotic sarcoma of the liver with brown ascitic fluid.

In cases of melanotic sarcoma of the liver the ascitic fluid may be clear and yet contain cells with pigment-granules inside them (Hektoen and Herrick[‖]). In a case under my care the ascitic fluid, though of the ordinary straw colour, really had melanogen in it, as shown by adding a watery solution of ferric chloride and getting a dark ring. On the other hand, Dr. Garrod tells me that in two similar cases with melanuria the ascitic fluid did not give the reaction.

In rare instances the ascitic effusion may be chylous as a result of transudation of chyle or even rupture of a lymphatic trunk, due to the pressure and obstruction exerted by a secondary growth in the course of the chyliferous trunks. A chyliform or fatty ascitic effusion, not due to the escape of chyle, but the result of fatty degeneration and disintegration of cells suspended in the peritoneal effusion, is not so rare. The fluid resembles chylous ascites to the naked eye, but differs from it microscopically in the size of the fat-globules, which are large and not in the fine emulsion characteristic of true chylous ascites. The oil-globules may be formed either in the cells of the growths and discharged into the peritoneal cavity, or in leucocytes. Corselli and Frisco * suggest that when malignant growths involve the peritoneum, toxic bodies are formed which induce degenerative changes in the cells suspended in the ascitic fluid and so lead to fatty ascites.

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[*] Bramwell, B.: Lancet, 1897, vol. i, p. 170.

[†] Hawthorne, C. O.: Clinical Jour., vol. viii, p. 361.

[‡] Legg: Trans. Path. Soc. London, vol. xxix, p. 225.

[§] Senator: Charité Annalen, 1890, Bd. xv, S. 261.

[‖] Hektoen and Herrick: American Journal of the Medical Sciences, vol. cxvi, p. 255, Sept., 1898.

In a case under the care of Dr. Whipham in St. George's Hospital a fatty effusion of a milky appearance was drawn off during life and was found at the autopsy to be associated with numerous secondary growths in the liver, which weighed 15 pounds; there was also a large growth involving the receptaculum chyli, but no rupture of lymphatic vessels was forthcoming. The primary growth was in the gall-bladder.

In other cases there is milky ascites in which the opalescence is due to the presence of nucleo-albumins and not to fat.

In a case of secondary carcinoma in a cirrhotic liver recorded by Achard and Laubry † the amount of fat—0.6 per cent.—was too slight to account for the milkiness of the ascites.

The number of leucocytes in the ascitic fluid may be so great as to suggest a purulent ascitic effusion without there being any sign of peritonitis.

This was evidently the nature of a case described as "Cancer nodulaire du Foie avec Ascite purulent" by Gentès,‡ for it is especially stated that there was no lymph or adhesions on the peritoneum.

As the result of perforation of a viscus or secondary infection, however brought about, an ascitic effusion in hepatic carcinoma may be genuinely purulent.

The blood shows diminution in the red cells, with a more marked diminution in the amount of hæmoglobin—a secondary anæmia. Leucocytosis may be present, but is not constantly found, and may be intermittent. It is usually moderate in degree.

In 14 cases examined by Cabot § leucocytosis was present in 8. In discussing leucocytosis in carcinoma of various organs Da Costa ‖ states that in his experience leucocytosis is more marked in hepatic carcinoma than in carcinoma of other organs.

The urine is usually diminished in amount, and occasionally shortly before death there may practically be suppression. It is high coloured, as a rule, and often lithatic, and may be of a rather high specific gravity. When there is jaundice, bile-pigment is usually found in the urine, but when the jaundice is very slight, it may be difficult or impossible to demonstrate its presence in the urine. When jaundice is marked, casts are found on centrifugalising the urine. Urobilin is found, and sometimes in increased quantities, unless the entrance of bile into the duodenum is entirely prevented. Indican is sometimes present.

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* Corselli and Frisco: Riforma Med., Roma, 1897, p. 278.

† Achard et Laubry: Bull. et Mem. Soc. Méd. des Hôp., April 25, 1902, p. 335.

‡ Gentès: Journ. de Méd. de Bordeaux, April 2, 1899.

§ Cabot: Clinical Examination of the Blood, p. 301.

‖ Da Costa: Clinical Hematology, p. 388.

Albuminuria is very rare in malignant disease of the liver, and its presence in a doubtful case is in favour of some other condition, such as lardaceous disease, renal tumor, cystic disease, or hydronephrosis. It may, however, be induced when the liver is so extensively infiltrated with growth that it is unable to stop poisons absorbed from the alimentary canal. The action of these poisons on the kidneys may result in albuminuria. In biliary obstruction with absence of bile from the intestines excessive fermentation may give rise to auto-intoxication and so to albuminuria. Teissier[*] has described this "hepatogenous albuminuria." As already pointed out, albuminuria is very rare in malignant disease of the liver, while these disposing conditions—hepatic insufficiency and jaundice—are fairly common; it would, therefore, appear that some other factor is necessary to produce albuminuria; the requisite factor is probably some primary feebleness or want of tone in the kidneys themselves.

Hydronephrosis may in rare instances be due to the pressure of the greatly enlarged liver on the right kidney. (Litten.[†]) When the liver is extensively infiltrated with growth, the amount of urea may be diminished, and leucin and tyrosin have been found in the urine, probably from cell destruction.[‡]

In melanotic sarcoma the pigment melanin may appear in the urine (melanuria). It has been said to be absent even when the liver is very extensively infiltrated with melanotic growth, but it is possible that it may be sometimes overlooked.

The urine, when passed, is generally of the ordinary colour and gradually darkens on standing and exposure to the air. This darkening may be brought about rapidly by the addition of an oxidising agent, such as bichromate of potash or nitric acid. A delicate test for melanin in the urine is the addition of a solution of ferric chloride, which even in dilute solutions produces a black colour; this reaction was discovered by von Jaksch[§] and Pollak[‖] in 1889. In some instances the urine is said to be black or dark brown when passed from the bladder; the colour is due to melanin. When the urine darkens after being passed the pigment is, we may suppose, at first in the form of a colourless chromogen—melanogen—which by oxidation yields melanin. The melanin from the growth passes into the circulation, and may either be excreted as such, blackening the urine, or it may be changed by the tissues into melanogen and not produce any very manifest alteration in freshly passed urine. Melanuria may thus escape notice unless the urine is kept for a time or acted upon by oxidising agents. Nepven and Chausel described pigment-granules in the blood and in the urine of patients with melanotic sarcoma.

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[*] Teissier: La Semaine Médicale, Aug. 23, 1899.

[†] Litten: Quoted in La Semaine Médicale, 1892, p. 80.

[‡] Compare Ulrich: Nordiskt. Med. Arkiv., 1896, No. 11.

[§] v. Jaksch: Zeitschr. f. physiolog. Chem., Bd. xiii, S. 385.

[‖] Pollak: Wien. med. Wochenschr., 1889, 39, 40, 41.

In a man, aged fifty-nine years, under my care in St. George's Hospital, there were extensive melanotic sarcomatous growths in the liver, which weighed 16 pounds. The primary growth was a melanotic sarcoma of the eye removed twenty months before at Moorfields; the urine was clear when first passed, but darkened on standing and on the addition of nitric acid and ferric chloride.

Melanuria very seldom or never occurs without secondary growths being found in the liver. The reasons for this probably are: (i) That there must be a considerable area of growth to provide a sufficiency of the pigment, and (ii) that the liver is involved more or less in most cases of generalised melanosis.

In one of the earliest cases described in this country as melanuria there was no hepatic growth (Hilton Fagge*), but it is possible that the pigment was not melanin, but methæmoglobin.

The occurrence of melanuria does not depend in any way on the presence of secondary growths in the kidneys and urinary tract; neither does it necessarily depend on the kidneys being healthy, for it has been observed when the kidneys showed the changes of arteriosclerosis. Cases have been observed in which melanuria has been said to be intermittent.

The presence of melanin or of melanogen in the urine may be of great use in arriving at an accurate diagnosis of a case of enlarged liver. Thus in cases where the primary growth in the eye remains latent, melanuria would show that the enlargement was due to a melanotic growth. It has been stated that melanin occurs occasionally in the urine in cases where no melanotic growth is present, but, as Garrod† has shown, this is a mistake and is due to large quantities of indican in the urine. It is, therefore, important to be on the outlook for the fallacy of mistaking indican for melanin. Urines which contain an excess of indican give with HNO_3 a reaction like that for melanin, but there is no colour reaction with ferric chloride, and in this way the two can be distinguished. The spontaneous darkening of the urine must be distinguished from that of alkaptonuria by the tests already given. In addition, the urine in alkaptonuria reduces Fehling's solution, but does not contain sugar, as shown by the phenylhydrazin test.

The toxicity of the urine has been found to be increased (Charrin ‡).

Œdema of the feet is comparatively frequent in the later stages of the disease. It may be due to several causes, such as cardiac debility, or to a toxæmic state resulting from hepatic insufficiency; in the latter case the œdema is analogous to that occurring in cirrhosis. Œdema, not only of the legs, but of the genitals, scrotum, and lower part of the trunk, may be mechanical and due to direct pressure exerted by growth, either in the liver or in the adjacent lymphatic glands, on the inferior vena cava and other venous channels, or to thrombosis of the inferior vena cava. (*Vide* case on p. 519.) It may also be due to the pressure of ascites on the inferior vena cava.

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* Hilton Fagge: Trans. Path. Soc., vol. xxviii, p. 172.

† St. Bartholomew's Hospital Reports, vol. xxxviii, p. 25.

‡ Charrin: Sem. Med., 1892, p. 80.

Thoracic Signs and Symptoms.—The large size of the liver may encroach on the thorax and thus lead to collapse and hypostatic engorgement of the bases of the lungs, with signs of bronchitis. Concomitant ascites will tend to displace the thoracic viscera and to compress the lungs and produce pulmonary embarrassment; this may be temporarily relieved by tapping the abdomen. When the growth involves the capsule of the liver or the diaphragm, it may give rise to the symptoms of pleurisy.

SYMPTOMS.

Great weakness, of which complaint is not infrequently made by patients, may be explained on one of the following hypotheses: It may be the result of such extensive destruction of the liver substance that the organ fails to do its work of stopping poisons which in the ordinary course of events are absorbed from the alimentary canal and then destroyed or rendered innocuous. This condition of hepatic inadequacy leads to general toxæmia and so to great feebleness and loss of appetite. Hepatic inadequacy would also interfere with the absorption and proper assimilation of food.

Gastric disturbance is frequent, there being loss of appetite, or even a marked distaste for food, especially for meat. In very rare instances there is great exaggeration of appetite, while in some cases the appetite remains unaffected or is sustained by a sort of auto-suggestion to counteract the wasting. (Hanot.*) Nausea is often present, and there may be actual vomiting, probably reflex in origin. Symptoms of chronic gastritis may for a time be the chief or only manifestations. The bowels are usually confined, and considerable difficulty may be experienced in the late stages in getting them to act without disturbing the patient too much. Diarrhœa is very exceptional. In the late stages obstinate hiccough may supervene, and may be very resistant to treatment.

Hepatic Pain.—The presence of growth in the liver gives rise to tension and stretching of the capsule and so to tenderness and to pain; this is further increased by perihepatitis set up by growths involving the capsule of the liver; when the growth is deep-seated in the substance, as in some examples of primary carcinoma, pain may be little marked or even absent. The pain may be almost constant in the right hypochondrium, but is often especially felt in the back, in the shoulder, or in the loins. It is more marked on exertion, and is worse at night. Pain is not always present, but it has some bearing on the diagnosis, since there is comparatively little pain in cirrhosis, while in malignant disease of the liver it is usually both persistent and severe. Secondary growths in the diaphragm or an extension of the growth from the liver into the diaphragm may set up pleurisy and so give rise to a good deal of pain. Attacks of pain resembling those of biliary colic, but not due to the passage of gall-stones, are occasionally met with when the common duct is pressed upon from without.

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* Hanot: Mercredi Médical, 1893, p. 417.

V. Schultz* describes attacks of pseudo-gall-stone colic in a man, aged forty-seven, who had secondary growths in the portal fissure compressing the duct and setting up jaundice. The primary growth was in the rectum.

Pruritus, or itching of the skin, the result of hepatic insufficiency, may be very troublesome, and a patient who is semicomatose may be continually scratching himself. Pruritus is usually seen in association with jaundice and comparatively late in the course of the disease. Bouchard† speaks of it as occurring sometimes early in the disease, before sufficient data for the diagnosis are forthcoming.

It is only very rarely that **peripheral neuritis** can be referred solely to failure of the detoxicating function of the liver. In most cases where peripheral neuritis complicates malignant disease of the liver it is due to concomitant alcoholism.

Hayem ‡ observed the acute onset of neuritis in both arms and legs in a case of primary carcinoma of the liver, which may have been due either to hepatic insufficiency or possibly to toxines derived from the growth.

In primary malignant disease the liver may be so extensively infiltrated with the growth that hepatic insufficiency is established. This form of auto-intoxication accounts for the occurrence of hæmorrhages, somnolence, and delirium in the last stages of the disease, and may render the diagnosis from cirrhosis difficult.

Charrin § described an exceptional case where mental delusions occurred in an early stage of carcinoma of the liver and were thought to be due to toxæmia, as the toxicity of the urine was increased.

DURATION.

In primary malignant disease of the liver the disease runs a rapid course, and sometimes justifies the description "acute cancer."‖

From an analysis of his cases Hale White ** concluded that the disease probably never lasts more than four months. In exceptional cases symptoms do not exist for as many weeks.

In secondary malignant disease of the liver the duration of life is variable. Much depends on the nature and situation of the primary tumor. This may kill the patient before the growths in the liver have become manifest. On the other hand, if the primary growth has been removed or remains entirely latent, life may be prolonged for a year, or, in extreme instances even longer, after signs of a growth in the liver have appeared. Usually, however, death occurs within six months of the first sign of hepatic enlargement.

Sometimes the liver may be considerably enlarged and nodular, and the patient remains for weeks in much the same condition and then suddenly goes rapidly down hill. It is often surprising how comparatively latent the disease may remain for a time. In other instances the liver steadily enlarges, and *pari passu* the patient's condition deteriorates. It has been stated that secondary growths in the liver grow with greater virulence during hot weather. (Fenwick.[*])

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* Schultz: Berlin. klin. Wochen., Feb. 5, 1894, S. 132.
† Bouchard: Congress at Rome, 1894.
‡ Quoted in Levi's Paris Thèse, 1896.
§ Charrin: Sem. med., 1892, p. 310.
‖ Rioufol, Thèse de Lyon, 1899. Acute Cancer of Liver.
** Hale White: Guy's Hospital Reports, 1890.

DIAGNOSIS OF MALIGNANT DISEASE.

The diagnostic signs of malignant disease in the liver are rapid and progressive enlargement, with evidence of definite tumor formation in the organ, pain, loss of weight and of constitutional strength, and, when the disease is not primary in the liver, evidence of malignant disease elsewhere. As has been pointed out already, the primary growth is latent in about half the cases of secondary malignant disease of the liver.

As a rule, malignant disease of the liver, whether primary or secondary, gives rise to some hepatic enlargement and pain, so that disease of the liver is at least suspected. When the growths are of small size and the liver is not enlarged, there may be no clinical evidence that the liver is affected; this occurs in a certain proportion of cases of secondary malignant disease of the liver, and is easily explained inasmuch as the patient dies from the effects of the primary growth.

In primary malignant disease of the liver it is rare for the growth to remain entirely latent. It may, however, happen that the observer's attention is exclusively directed to secondary results or concomitant affections.

Thus Sokoloff[†] describes the case of a man aged seventy who had ascites and dropsy and was regarded as having arteriosclerosis. After death a primary columnar-celled carcinoma of the liver was found. Gouget[‡] narrates a very similar case in a man aged fifty-three years, thought to have arteriosclerosis and bronchitis. At the autopsy the liver was of normal size and contained numerous growths of columnar-celled carcinoma; there were no other growths in the body. To the naked eye the growths closely resembled gummata. H. G. Wells[§] reported a case of primary carcinoma with cirrhosis which was latent, the patient dying from uræmia.

Hale White[‖] records the case of a woman aged thirty-nine who was thought to be suffering from the vomiting of pregnancy, but who died after premature labour had been induced. Primary malignant disease of the liver, weighing 126 ounces, was found.

DIFFERENTIAL DIAGNOSIS.

Under this head the diagnosis of malignant disease in the liver substance, whether primary or secondary, from other conditions will first be considered, and then the distinction between primary and secondary malignant disease will be dealt with.

Portal Cirrhosis.—When a patient comes under observation with the abdomen full of ascitic fluid it is often difficult to form a reliable opinion as to whether there is cirrhosis in a late stage or malignant disease of the liver. The diagnosis must then remain in doubt until the fluid is withdrawn; when this has been done, the liver can be carefully examined.

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[*] Fenwick: Cancer and Other Tumors of the Stomach, p. 183.

[†] Sokoloff: Virchow's Archiv, Bd. clxii, S. 1.

[‡] Gouget: Bull. Soc. Anat. Paris, 1898, p. 605.

[§] Wells, H. G.: American Journ. Med. Sciences, vol. cxxvi, p. 403, 1903.

[‖] Hale White: Trans. Path. Soc., vol. xxxvi, p. 251.

A small or moderately enlarged liver, when associated with enlargement of the spleen, points to cirrhosis, while a large and nodular liver, especially when combined with umbilication of the surface, indicates malignant disease. Emaciation and pain are more prominent in malignant disease, but wasting may be very considerable in cirrhosis. A large cirrhotic liver, when associated with some jaundice and ascites, closely imitates carcinoma, but in cirrhosis the enlargement is more uniform, and affects both lobes, while the spleen is often enlarged and cachexia is less rapid. The association of well-marked jaundice and ascites, however, should always suggest secondary malignant disease. Progressive increase in size is in favour of malignant disease, more especially if it affect one lobe only. In the following case primary carcinomata imitated cirrhosis:

A cook aged forty-three years was admitted under Dr. Penrose into St. George's Hospital with "a lump in the middle of the abdomen," vomiting in the morning, loss of appetite, and emaciation. She had had piles for fifteen years. Alcohol had been taken in moderation. On admission she was thin, had an enlarged, roughened liver, and some ascites, which rapidly increased in amount and required tapping. She became jaundiced and passed into a "typhoid" condition, with dry tongue, muttering delirium, and running pulse. At the autopsy, except for a few minute growths in the lungs, there was no new-growth in any part of the body, except in the liver, which weighed 106 ounces; there was no growth in the gall-bladder or ducts; the right lobe contained extensive areas of whitish-yellow growth of firm consistency, and also small separate umbilicated growths; the left lobe was a thin, small cake of about the size of a child's hand, and was nearly separated from the rest of the liver, and moved on a hinge; it also contained much growth. The liver was not cirrhotic. There was chronic gastritis.

In the rare condition, primary carcinoma supervening on cirrhosis, a diagnosis from cirrhosis is usually impossible, though in a few cases where the liver is large the nodules of growths can be felt. Pain over the liver is often a more prominent feature in these cases than in cirrhosis, and jaundice, though not always present, may be very marked.

From the large liver of **hypertrophic biliary cirrhosis** primary malignant disease differs in its more rapid growth, in the absence of splenic enlargement, and in the character of the jaundice. In malignant disease it is, generally speaking, either absent or, if present, obstructive, so that no bile passes into the blood. In biliary cirrhosis jaundice is constant, but not complete, and the fæces are not devoid of bile. Hypertrophic biliary cirrhosis is met with much earlier in life than malignant disease.

Syphilitic Disease of the Liver.—Gummata and gummatous enlargement of the liver, especially when the patient is markedly cachectic, very closely imitate malignant disease of the liver. In cases where the liver is hard and enlarged and the patient's general condition is good, gummata should be thought of and vigourous antisyphilitic treatment should be employed. In all cases of doubt iodides in large doses should be given. If, after a full course, the enlargement is still progressive, the case is almost certainly malignant. A history of syphilis is, of course, important, but the most decisive point is the effect of antisyphilitic treatment adequately carried out.

A large, firm, **lardaceous liver** in a cachectic patient might be mistaken for primary massive carcinoma of the liver at first sight, but the evidence of lardaceous disease elsewhere, as shown by albuminuria and diarrhœa, the absence of pain and of rapid and progressive enlargement of the liver, together with a history of past suppuration or of syphilis, should enable the practitioner to come to a correct diagnosis. When gummata are combined with the lardaceous change, the liver, being nodular and enlarged, may resemble that of secondary malignant disease. The history and evidence of syphilis are important, but the effect of treatment is the only really reliable means of definitely deciding the point; if the liver progressively enlarges under full doses of iodide of potassium, malignant disease is almost certainly present. A lardaceous liver with syphilitic cicatrices and copious adhesions sometimes feels so irregular through the abdominal wall that malignant disease is likely to be diagnosed; other evidences of lardaceous disease, such as albuminuria, should always be looked for in doubtful cases of malignant disease of the liver. Albuminuria is decidedly rare in the latter disease.

A hydatid cyst may imitate malignant disease of the liver, especially a primary massive carcinoma, in a comparatively early stage before marked constitutional symptoms have arisen, while multiple hydatid cysts may simulate the nodules of secondary malignant disease.

In hydatid the enlargement is slow and constitutional symptoms are absent. In malignant disease the tumor usually grows rapidly, other nodules may be felt, and cachexia is likely to supervene. Generally speaking, malignant disease occurs later in life than hydatid; caution is, therefore, necessary before diagnosing a hydatid cyst of the liver in elderly persons. These points are illustrated in the following case of primary massive carcinoma of the liver:

A man aged sixty-five was admitted under my care in St. George's Hospital in September, 1900, with a lump in the situation of the left lobe of the liver, dull pain of three months' standing in the epigastrium, which was getting worse, and loss of flesh. There was no history of syphilis and no evidence of growth elsewhere. The diagnosis lay between malignant disease, gumma, and hydatid. A full course of iodides did no good, and in the middle of October the liver was bigger and definite nodules could be felt on the surface. The liver rapidly enlarged in size, and the patient lost flesh and weight. Pain was pretty constant over the liver, which eventually nearly filled the abdomen. There was never any ascites, and jaundice only occurred three days before death. No rise of temperature was ever observed. During the last twenty-four hours of life only 3 ounces of urine were passed. At the autopsy the liver showed a massive growth in the left lobe, of firm consistence and bright yellow colour, which involved the capsule and was firmly adherent to the stomach. There were numerous secondary growths in the right lobe, which was smaller than the left. The gall-bladder was very small and collapsed, but not involved in the growth. There was considerable enlargement of the glands in the portal fissure, but no obstruction of the portal vein or bile-ducts. The liver weighed 8 pounds. No growth could be found in any other part of the body. Microscopically the growth was a spheroidal-celled carcinoma and probably arose from the liver cells. The fibrous tissue of the growth was in places very profuse, and the epithelial cells were much compressed; it resembled a slow-growing carcinoma of the breast. The fibrous tissue showed advanced hyaline change.

When the liver contains several hydatid cysts, some difficulty in arriving at a correct diagnosis must be expected.

Thus in a case diagnosed as hydatid of the liver and operated upon, the appearances so closely resembled multiple malignant growths that the operation was abandoned; at the autopsy they were found to be multiple hydatids after all. (Sargnon.*) The coincidence of carcinoma and hydatid cysts in the same liver has several times been met with. (Habran,† Longuet,‡ Florand.§)

Multilocular or alveolar hydatid has often been mistaken for malignant disease, both clinically and even when found after death. It has not been described as occurring in England, and it is rare anywhere. In most cases of the disease the spleen is enlarged, while the course of the disease is much slower than in malignant disease.

From Intra-hepatic Suppuration.—In rare instances the soft character of a rapidly growing tumor, or the formation of false cysts from necrosis or hæmorrhage, may give rise to fluctuation, while fever, which is not very uncommon in malignant disease of the liver, may further increase the resemblance to some form of intra-hepatic suppuration, such as abscess, pylephlebitis, etc. An exploratory laparotomy may be the only means of distinguishing between growth and suppuration. Suppuration may indeed be superimposed on malignant disease.

In the following case abscess seemed clinically to be more probable than growth or cirrhosis:

A man aged forty-one years began to suffer from sick headaches three months before his death; a month later he had flatulence and epigastric pain. When admitted into St. George's Hospital on Feb. 12, 1902, under my colleague, Dr. Ewart, the patient, who was well nourished and free from jaundice, presented great enlargement of the liver, which projected markedly in the epigastrium. After admission the temperature became raised, and, an abscess being suspected, the liver was aspirated, but nothing but blood was withdrawn. As the temperature continued to rise, Sir W. Bennett opened the abdomen and found numerous growths on the surface of the liver. A small piece was removed, and found to be a spheroidal-celled carcinoma. The patient died a week later. At the autopsy the liver weighed 11 pounds 7 ounces; the left lobe was almost uniformly infiltrated by new-growth, while the right lobe contained a number of discrete growths. The only other growth was one in the middle of the body of the pancreas.

Howard Marsh ‖ reported the case of a soldier aged forty-three, who had been in India, and had an enlarged liver extending two inches below the ribs and forming a prominent swelling in the epigastrium, with exactly the appearance of an abscess pointing; it was soft, fluctuating, and the skin over it was dusky-red. Aspiration only brought away a little blood, and at the necropsy cancer of the liver was found. In Bramwell and Leith's ** case of primary sarcoma of the liver an abscess was diagnosed and 53 ounces of chocolate-coloured fluid were removed by aspiration. There was a primary, irregular-celled sarcoma of the liver, which weighed nine pounds. Hawthorne †† has published a somewhat similar case.

In the following case there was some resemblance to pylephlebitis:

A man aged twenty was admitted under my care at St. George's Hospital on May 15, 1902, with anæmia, fever, and a large and tender liver. His history pointed to an attack of appendicitis five weeks before, followed by two rigors and by vomiting. It was thought that he had either a large abscess in connexion with the vermiform appendix and tracking up to the liver by the side of the colon, or pylephlebitis. It was decided to give him the benefit of the doubt and he was advised to submit to operation. At the operation by Mr. Jaffrey there was no abscess, but the liver was large and bled readily when punctured; on the convexity of the liver there was a raised area, thought to be either an early stage of an abscess or new-growth. It was punctured, but nothing came out. The age of the patient militated against new-growth. The abdomen was closed, and the patient survived for five weeks; during the greater part of this period the temperature was intermittent, going up to 101° at night and becoming normal in the morning; during the last week of life the temperature was almost normal. Œdema of the legs and back developed some weeks before death.

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* Sargnon: Lyon Médical, 1898, p. 254.
† Habran: Bull. Soc. Anat., 1868, p. 437.
‡ Longuet: Gaz. hebdom., 1874, p. 774.
§ Florand: Bull. Soc. Anat., 1886, p. 677.
‖ Marsh, H.: St. Bartholomew's Hospital Reports, vol. xxiii, p. 148.
** B. Bramwell and Leith: Lancet, 1897, vol. i, p. 170.
†† Hawthorne, C. O.: Clin. Jour., vol. viii, p. 361.

At the autopsy the liver was occupied by numerous white growths showing cystic degeneration, and weighed 18 pounds. The primary growth was in the left kidney. There was thrombosis of the inferior vena cava close to its bifurcation, thus accounting for the œdema. The portal vein was normal.

Microscopically the growth was an endothelioma with much myxomatous change.

A large cystic sarcoma of the liver, such as is described on page 517, may very closely imitate an abscess or a sanguineous peritoneal cyst. If opened, the fluid from a cystic sarcoma will probably contain growth which, when examined, microscopically, will show evidence of malignancy, but even then it may be impossible to say whether the growth arose in the liver or invaded it, as a suprarenal or other retroperitoneal tumor might do. The diagnosis during life in these cases, which luckily are rare, is extremely difficult. Conversely, slow abscess formation in the liver may be regarded as malignant disease and not operated upon for this reason.

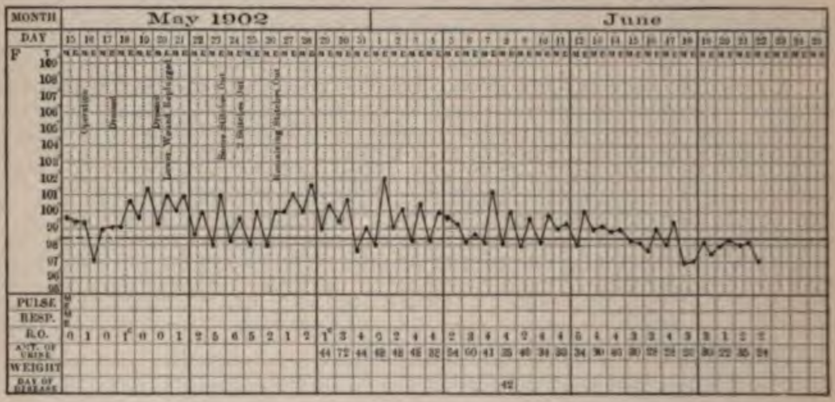

FIG. 71.—TEMPERATURE CHART OF MAN, AGED TWENTY YEARS, WITH SECONDARY ENDOTHELIOMA OF LIVER IMITATING PYLEPHLEBITIS. PRIMARY GROWTH IN THE LEFT KIDNEY.

Chronic Venous Engorgement.—The enlarged and tender liver of chronic venous engorgement, especially in the late stage of mitral disease, has, in rare instances, been regarded as malignant. This mistake is not likely to occur often, as the general aspect of the two diseases is so different. Difficulty is more likely to arise in cases of marked dilatation of the left ventricle without any mitral murmur. The presence of obstructive cardiac or pulmonary disease, and the effect of treatment by digitalis, strophanthus, purgatives, etc., in diminishing the size of the liver are points in the diagnosis on which further insistence is unnecessary.

A woman, aged forty years, but looking fifteen years older, was admitted under my care in St. George's Hospital in January, 1903, in great pain and respiratory distress. Her appearance suggested morbus cordis or a large pleural effusion, but the heart appeared healthy and there was only a little dulness at the right base. There was much resistance in the epigastrium and great pain on pressure, and as she had frequent retching, it was thought she might have malignant disease of the stomach and liver. Her condition prevented a thorough examination, and she was kept under the influence of morphine, but the pain seemed very severe. Three days before death she became jaundiced. At the autopsy there was no growth of any kind. The liver was enlarged and showed some, but not advanced, chronic venous engorgement. The heart weighed 15 ounces and showed extensive fibroid disease. The orifices of the coronary arteries were extremely small, and the ascending part of the aorta showed gelatinous thickening, suggesting syphilitic or acute aortitis. There were a pulmonary apoplexy in the right lung and a pleural effusion. It is probable that the pain was cardiac and of the nature of angina.

Impacted Gall-stone in the Common Bile-duct; Intermittent Hepatic Fever.—Impaction of a gall-stone in the common bile-duct may occur without any previous attacks of biliary colic. When this occurs in a person past middle life, it may resemble very closely malignant disease of the liver, especially that form arising in the bile-ducts (*vide* p. 683). As time goes on, however, the jaundice tends to diminish, whereas in malignant disease it becomes deeper. In impacted gall-stone the liver, if enlarged at first, does not progressively increase in size, but rather diminishes, and there is an absence of irregularities on its surface.

A man aged sixty-seven became jaundiced at the beginning of 1890 after having felt weak for ten days; there had been no pain or colic. About May 17th he consulted the late Sir Andrew Clark, who, according to the patient, diagnosed cancer of the liver and gave him a month to live. When admitted to St. George's Hospital under the late Dr. Cavafy he was thin, jaundiced, and weak. The hepatic dulness began at the fifth rib in the right nipple line, and extended below the right costal margin, where there was a rounded, dull swelling extending downwards to within one inch of the umbilicus. No pain or tenderness existed. With rest in bed the jaundice cleared away and the tumor in the right hypochondrium receded, until, at the beginning of August, the skin was almost natural in colour. He then had spells of diarrhœa, which, however, were easily controlled by treatment. On September 20th and October 8th he had definite rigors, his temperature was raised at intervals, and he was losing flesh and strength from attacks of diarrhœa. On November 17th a severe bout of diarrhœa began; on the 19th he had a rigor, and on the following morning he died rather suddenly. At the autopsy I found a large calculus in the common bile-duct, close to the duodenum; it was loose and allowed bile to flow past it into the duodenum, as was proved by pressure on the gall-bladder. There was catarrhal cholangitis, to which the fever and occasional rigors were due; the liver showed secondary pericholangitic fibrosis and there were numerous old adhesions around the gall-bladder and liver. There was no trace of malignant disease in the body.

A displaced or a wandering liver very rarely imitates malignant disease. In Crawfurd's * case of anteverted wandering liver malignant disease was diagnosed during life. The association of jaundice and ascites with hepatoptosis is most unusual, but it may occur from kinking of the portal vein and bile-duct. The freely movable state of the liver should direct attention to the real condition. The severe constitutional symptoms in malignant disease and their absence in wandering and displaced livers should help to prevent any chance of confusion.

A large renal tumor on the right side may appear to be in direct continuity with the liver. In some cases of extensive **cystic disease** of the kidneys the tumor may imitate a distended gall-bladder, or possibly, if tense cysts project from the surface of the kidney, secondary growths in the liver. A bimanual examination will show that the renal tumor definitely bulges into the loin. The presence of bowel in front of the renal tumor is important; this may be made more manifest by filling the colon with air after removing its solid contents by means of an enema.

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* Crawfurd, R. P.: Lancet, 1897, vol. ii, p. 1182.

Tumors of the right suprarenal body, by growing forwards, may very closely resemble hepatic growths. In some cases the liver may become invaded by continuity and secondary growths often occur in the liver.

In a large cystic sarcoma of the right suprarenal body, which I examined postmortem in 1891, the diagnosis was first hydatid of the liver, and subsequently malignant disease; in this case there were secondary growths in the liver, as well as direct invasion of that organ.

Inflammatory thickening around the gall-bladder may be palpable as a hard mass, and thus may give rise to physical signs resembling carcinoma. The history of gall-stones and the fact that the patient's general state is not so grave as in carcinoma are important points to bear in mind.

Occasionally **fæcal accumulation** in the transverse colon may imitate malignant disease; here the tumors may vary in position from time to time, can be indented by pressure, are capable of removal by purgatives or abdominal massage, and, when a careful examination is made, if need be under an anæsthetic, other masses can be made out in the course of the colon.

Improbable as it may appear, difficulty has arisen in distinguishing between *pregnancy* and secondary malignant disease of the liver.

In the following case* both conditions existed at the same time and the abdominal enlargement was naturally thought to be explained by pregnancy. A married woman aged thirty-nine years, who had had several children, was thought to be pregnant. She died, and a six-months fœtus was found in the uterus. The liver weighed 17½ pounds and contained numerous secondary growths; the primary growth appears to have been in the colon.

A case was reported by Hale White† in which a woman was thought to be suffering from the vomiting of pregnancy until a primary carcinoma of the liver was found at the autopsy.

DIAGNOSIS BETWEEN PRIMARY AND SECONDARY MALIGNANT DISEASE OF THE LIVER DURING LIFE.

In secondary malignant disease of the liver the primary growth may remain latent and not give rise to any symptoms during life. In such cases there are often no means of arriving at a correct diagnosis of secondary, rather than primary, malignant disease of the liver. These cases, which are clinically described as "malignant disease of the liver," tend, when included in statistics, to make primary malignant disease appear less rare than it really is. According to Hale White,* in about half the cases of secondary carcinoma of the liver the primary site cannot be determined during life.

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* Robinson: Trans. Path. Soc., vol. ii, p. 167.

† Hale White: Trans. Path. Soc., vol. xxxvi, p. 251.

The primary growth may remain latent when it is in the stomach, pancreas, œsophagus, kidney, and, in exceptional instances, when in the colon.

In the following case the primary growth was entirely latent, the liver was greatly enlarged, and nodules were easily felt; the disease of the liver was regarded as secondary, possibly, to a gastric carcinoma.

A wasted old man aged sixty-two years was admitted under my care in St. George's Hospital on June 22, 1899, complaining of pain over the liver, inability to lie on his left side, shortness of breath, difficulty in digestion, and constipation. Six weeks previously his legs began to swell; this was followed by swelling of the abdomen. He had ascites which required tapping. The liver was much enlarged, and extended nearly down to the umbilicus; nodules which seemed to be umbilicated were readily felt. On the skin over the free edge of the liver there was a meshwork of dilated vessels. There was dulness in both flanks. The urine was free from albumin; two days before his death, when his conjunctivæ became jaundiced, bile-pigment appeared in the urine. He got steadily weaker, had little or no pain, completely lost his appetite, and died after being in a drowsy condition for forty-eight hours on July 6th. At the autopsy the liver weighed 9 pounds 14½ ounces, and was packed with nodules of soft white growth which were not umbilicated. The right kidney weighed 8 pounds 5½ ounces and was transformed into a large hæmorrhagic growth which had broken down into pseudo-cysts. Some of the cysts contained cholesterin crystals. Microscopically the growth was a beautiful villous carcinoma. (*Vide* Fig. 66.)

Kelynack† has described an almost exactly similar case in a woman, but the left kidney was affected and there was hæmaturia, so that the primary growth did not remain latent as in this case. The liver contained numerous cystic growths and weighed 111 ounces.

I have seen two other cases in which the primary growth in the kidney remained quite latent; this is very likely to happen when the right kidney is affected, and is under cover of the enlarged liver, but it may occur when the growth in the left kidney is small.

From extreme sensibility and a mistaken sense of delicacy a woman may conceal the fact that she has carcinoma of the breast and only complain of symptoms pointing to malignant disease of the liver.

Such a case is recorded by Pearson and Howes‡ where an ulcerating carcinoma of the mamma was only discovered after death in a woman aged sixty who during life had been under treatment for a tumor in the liver with pain and ascites.

Carcinoma of the stomach may remain quite latent when there are extensive secondary growths in the liver. According to Fenwick,§ the changes in the liver are most marked when the growth in the stomach is comparatively insignificant. Inasmuch as a pyloric growth is likely to lead to obstruction and symptoms, the latent growths are more often in the body or cardiac end of stomach.

Secondary growths in the liver are not uncommon when carcinoma attacks the lower half of the œsophagus, but dysphagia is nearly always present.

In a man aged fifty-five years who died in St. George's Hospital with carcinoma of the œsophagus and numerous secondary growths in a liver weighing 14 pounds, there was nothing more definite than a distaste for solid food.

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* Hale White: Allbutt's System of Medicine, vol. iv, p. 197.

† Jour. Path. and Bacteriol., vol. iv, p. 236.

‡ Trans. Path. Soc., vol. xxvi, p. 185.

§ Fenwick: Cancer and Other Tumors of the Stomach, p. 182.

The presence of an enlarged gland (Virchow's gland) above the clavicle should suggest the possibility of œsophageal carcinoma, but it may, of course, occur in other cases of generalised new-growth. Enormous enlargement of the liver may be due to melanotic sarcoma arising secondarily to a primary growth in the uveal tract; in such cases the seat of the primary growth may easily be overlooked if the patient wears a glass eye and does not call attention to the fact that his eye has been removed.

Multiplicity of nodules on the surface of an enlarged liver is much in favour of secondary growth, but unless there is definite evidence of primary growth in the body, or of one having been removed, the diagnosis of secondary growths, though most probable, cannot be made with absolute certainty, since primary malignant disease may occur in a multiple nodular form. Deep jaundice and the association of ascites with jaundice are in favour of secondary malignant disease, while very rapid enlargement of the liver without emaciation is more frequent in primary malignant disease. It is true that the liver may increase in size very rapidly in secondary malignant disease, but since the primary growth is usually in the alimentary canal, there is generally considerable emaciation on this account before the liver is much or at all affected. When the primary growth is in the kidneys or in the uveal tract, emaciation is not so marked. In the enlargement of the liver due to melanotic sarcoma a clue to the nature of the disease, even in the absence of any history of an intra-ocular growth, may be obtained by finding melanin in the urine.

To summarise the differential diagnosis of primary and secondary malignant disease of the liver:

Primary.	*Secondary.*
No sign or symptom of growth elsewhere in the body.	Some evidence of growth elsewhere.
A single tumor.	Multiple tumors.
Very rapid growth.	Less rapid growth.
Jaundice rare and slight.	Jaundice common.
Ascites infrequent.	Ascites common.
Emaciation not so marked.	Emaciation marked.
Course rapid.	Course not so acute.

Pepere * has attempted to draw a clinical distinction between primary carcinoma and primary sarcoma of the liver. According to his observations, primary sarcoma runs a more rapid course and is less frequently accompanied by jaundice or ascites than primary carcinoma.

PROGNOSIS.

When the diagnosis of malignant disease of the liver can be made at the bedside, the prognosis is always hopeless. It is true that when laparotomy reveals the presence of early primary malignant disease of the liver, malignant disease limited to a constriction lobe, or malignant disease of the gall-bladder invading the liver, there is a chance that re-

* Pepere: Archiv. de Méd. expériment. et d'anat. path., tome xiv, p. 805, Nov., 1902.

moval will not be followed by recurrence. But even in these cases, which can hardly be diagnosed with any certainty before the abdomen is opened, the disease usually returns and kills the patients. Operation for removal of malignant growths from the liver, whether from its substance or when starting in the gall-bladder, is the only means at our disposal at present of mitigating the otherwise absolutely fatal prognosis. The prognosis is better when a growth originating in the gall-bladder is removed than in resection of the liver for a primary neoplasm. Death is more rapid in primary malignant disease than in the more familiar secondary growths in the liver.

How long life may be prolonged with secondary growths in the liver is uncertain. In most cases death follows within six months of definite evidence of hepatic enlargement. It must be remembered that in some instances the liver may have been previously enlarged from some independent cause; a floating lobe or tight-laced liver might thus give rise to a fallacy.

In a case of secondary melanotic sarcoma of the liver recorded by Litten there was evidence of hepatic enlargement for four years before death, a period quite incompatible with the view that a secondary growth was present all the time.

On the analogy of the spontaneous disappearance of solid and inoperable growths in the abdomen having the appearance of malignancy —a remarkable event to which the late Professor Greig Smith * drew attention—it is conceivable that malignant disease of the liver might occasionally disappear. Undoubted carcinomatous secondary growths in the skin have in very rare instances been known to disappear spontaneously,† and in a similar case enlargement of the liver has been noticed to pass away. (A. P. Gould.‡)

Campbell quotes a case § in which influenza, supervening in the course of malignant disease of the liver, was followed by rapid diminution in the size of the liver. The patient indeed seemed to get well, but in one and a half years' time the growth returned and proved fatal. It is possible that in this instance a secondary streptococcal infection on the influenza attack may have manufactured a toxine that acted on the hepatic growth, much in the same way as Coley's fluid does on sarcomata.

The only bright side to the prognosis of malignant disease of the liver is the possibility that the diagnosis may be wrong and that the actual condition is gummatous or hydatid disease of the liver.

TREATMENT.

The medical treatment is purely palliative, and directed chiefly to the relief of pain and discomfort by morphine, opium, and chloral. Hypodermic injection of morphine is preferable to opium by the mouth, inasmuch as it is more surely absorbed, disturbs digestion less, and its effects can be more accurately estimated. From the necessarily fatal nature of the disease morphine may be given without any qualms of conscience as to morphinomania. Measures should be taken to combat the excessive constipation induced by morphine, and it is often advisable to combine the morphine with a little atropine.

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* Greig Smith: Medico-Chirurg. Trans., vol. lxxvii, p. 139.
† Gould, A. P.: Trans. Clin. Soc., vol. xxx, p. 205.
‡ Gould, A. P.: Clinical Journ., 1902, May 28, p. 96.
§ Campbell, H.: Brit. Med. Journ., 1898, vol. i, p. 1126.

Pain over the liver may be to some extent relieved by the local application of a plaster made up of the pharmacopœial plasters of opium and of belladonna. Hot fomentations or poultices may be given a trial. The pain and tenderness are, of course, aggravated by examination, which should, therefore, not be unnecessarily repeated.

If there is jaundice, itching may be the chief thing that the patient complains of, and, to relieve it, chloride of calcium by the mouth should be tried, while warm alkaline baths, bathing the skin with carbolic acid 1 : 40, or the hypodermic injection of pilocarpine, may give relief; probably morphine will be found to be the most generally successful means of combating it.

Vomiting should be treated by ice, morphine, bismuth, and dilute hydrocyanic acid. Washing out the stomach may be very useful.

Flatulence and distension of the intestine should be treated by various carminatives, by minute doses ($\frac{1}{40}$ gr.) of calomel, creasote perles, and by gentle purges. Constipation should be met by saline purges and mild laxatives, such as cascara.

The diet is largely determined by the patient's inclinations; usually there is want of appetite and dislike for meat, so that liquid food, milk, jellies, tea, and coffee are all that he cares to take. Milk has the advantage of being easily digested and giving rise to a minimum of putrefactive products. Stimulants are usually desirable.

If ascites gives rise to abdominal distension and discomfort, tapping should be performed.

Operative Treatment.—Removal of the growth is, of course, the ideal method of treatment, but is only to be thought of for a primary and single growth. A number of cases have been operated upon and excision of the malignant growth performed.

In a tabular statement of 76 cases in which resection of the liver had been performed for growths or other conditions, Keen* gives 18 carcinomata, 5 sarcomata, and 1 endothelioma.

Removal of a malignant growth in the gall-bladder is much less difficult than excision of a primary malignant growth from the substance of the liver. Another grave practical difficulty is that of arriving with any certainty at a diagnosis of a primary hepatic growth before it has become too extensive for satisfactory removal.

Success is, therefore, more likely to occur in cases where the exploratory operation was undertaken under the idea that there were conditions other than malignant disease present, such as a hydatid cyst. It is very probable that good results might follow in cases where a small secondary growth is excised at the same time as a primary carcinoma of the stomach or of the gall-bladder, as in Mayo Robson's case,† where complete recovery followed, is removed. But in such cases there is, unfortunately, the danger of the liver being more widely infected than appears to the naked eye.

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* Keen: Annals of Surgery, Sept., 1899, p. 276.

† Mayo Robson: Medico-Chirurg. Trans., vol. lxxix, p. 159.

Laparotomy, with a view of removing a diagnosed growth, would often be only an exploratory incision, for the extent of the disease and the presence of secondary growths would, in a large number of cases, render any operative treatment impracticable. At the present time, however, the surgery of the liver is advancing by such leaps and bounds that the value of resection of the liver for new-growths is likely to be more extensively tested. According to H. J. Waring,* most of the cases that have been operated upon have died from a recurrence of the growth.

* Waring, H. J.: Diseases of Liver, Gall-bladder, etc., p. 195.

JAUNDICE.

Definition.—Jaundice is the condition due to the presence of bile-pigment in the blood, and is recognised clinically by staining of the skin, conjunctivæ, mucous membranes, blood-serum, and, as a rule, of the urine, by bile-pigment.

Like albuminuria, it is a symptom and not a disease, and may be met with in a number of different conditions, the common and essential factor being obstruction at some point to the passage of bile along the bile capillaries or ducts.

Etymology.—The word jaundice is derived from the French *Jaune*, yellow. Wickham Legg * gives a number of possible derivations for icterus, such as ἴκτις, the yellow-breasted martin, which probably was the equivalent in ancient Greek households of our domestic cat; ἴκτερος, the golden oriole, the sight of which was supposed to cure jaundice, while the bird died (Pliny); and from ἴκτινος, a kite, from the colour of its eyes.

INTRODUCTION.

The formation of bile-pigment from hæmoglobin is limited to the cells of the liver and cannot be vicariously carried out elsewhere in the body, for, as shown by experiments on animals, this transformation does not take place when the liver is removed or, and this comes to the same thing, when all the vessels going to it are ligatured.

Moleschott † showed that after excision of the liver in frogs there was no formation of bile in any part of the body; while by excluding the liver of pigeons from the circulation by ligature of its vessels Stern ‡ and Minkowski and Naunyn,§ in ducks, proved that the same was true in birds.

It was, however, formerly thought that since hæmatoidin, which is chemically identical with bilirubin, is formed in old hæmorrhages, etc., from hæmoglobin, bile-pigment was similarly manufactured in other parts of the body.

Jaundice, or the presence of bile-pigment in the blood, is due to the passage of bile, manufactured by the liver, into the circulation instead of into the intestines. This miscarriage of the bile may occur either directly the bile-pigment is formed by the liver cells—*i. e.*, before the bile enters the bile-ducts—or later, after it has passed into the ducts. In cases of long-standing biliary obstruction, in which the dilated intrahepatic ducts only contain mucus, the bile formed by the liver cells passes almost directly into the adjacent lymphatics, and thence into the thoracic duct, and so reaches the general circulation. Cases of this kind, in which no bile is visible in the ducts, were formerly thought to prove that jaundice might result from suppression of the bile-secreting function of the liver, and might be due to the resulting accumulation in the blood, of bile-pigments formed in the circulation from hæmoglobin. This, however, is erroneous, for the presence of bile-pigment in the liver cells in such cases shows that the formation of bile still continues. When there is obstruction in the ducts the bile passes from the bile capillaries or ducts into the lymphatic vessels of the liver and not into the blood-vessels. This has been shown by the experiments of Saunders * early in the last century (1803), and later by Fleischl † (1874), V. Harley ‡ (1892), and Szubinski § (1899). It has also been shown that jaundice due to ligature of the bile-duct may be removed or prevented by ligature of the thoracic duct.

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* Legg, J. Wickham: Bile, Jaundice, and Bilious Diseases, p. 225.

† Moleschott: Archiv f. physiol. Heilk., Bd. xi, S. 479, 1852.

‡ Stern: Archiv f. exper. Path. u. Pharmak., Bd. xix, S. 39.

§ Minkowski and Naunyn: Archiv f. exper. Path. u. Pharmak., Bd. xxi, S. 1.

It was thought by Frerichs, and quite recently by Szubinski, that under certain conditions the normal mechanism of secretion of bile by the liver cells may be so disordered that, instead of turning sugar into the blood and bile into the bile capillaries, the bile is discharged directly into the blood.

Obstruction to the flow of bile through the ducts leads to a rise in the pressure of the bile, which is normally low, and, as a result, the bile passes into the lymphatics and so into the general circulation. This clearly explains the production of jaundice in cases where there is a gross mechanical obstruction in the ducts, but it is necessary to consider further the method of causation of jaundice in those cases where there is no manifest obstruction in the larger bile-ducts.

PATHOLOGY OF JAUNDICE.

Jaundice was formerly divided into: (i) Hepatogenous or obstructive, due to manifest obstruction in the larger bile-ducts, and (ii) so-called non-obstructive, where there was no gross obstruction in the course of the bile-ducts. This form included (*a*) jaundice thought to be due to hæmolytic changes in the blood, which consisted in the liberation of hæmoglobin and its transformation in the circulation into bile-pigment; this was spoken of as *hæmatogenous jaundice*. (*b*) *Jaundice from polycholia*, in which an excessive secretion of bile was followed by such free absorption of bile by the mucous membrane of the intestine and bile-passages that some of it overflowed into the general circulation. (*c*) *Jaundice by suppression*, in which the cells of the liver were supposed to strike work and no longer form bile. As a result an accumulation of bile-pigments, manufactured in the general circulation, was thought to occur. As in the first-mentioned form (hæmatogenous jaundice), this explanation was based on the erroneous assumption that bile-pigments could be formed elsewhere in the body than in the liver.

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[*] Saunders: A Treatise on the Structure, Economy, and Diseases of the Liver, 1803, p. 3, 3d ed.

[†] Fleischl: Arbeiten aus d. Anstalt zu Leipsig, 1874, Jahrg. ix, S. 24.

[‡] Harley, V.: Archiv f. Anat. u. Phys., 1893, S. 291.

[§] Szubinski: Ziegler's Beiträge, Bd. xxvi, S. 446, 1899.

"Hæmatogenous" Jaundice.—In various toxic and infective conditions of the blood in which the hæmoglobin is liberated from the red blood-corpuscles jaundice of a slight degree of intensity is often seen. A good example of this "toxæmic" jaundice is provided in the experiments of Stadelmann* and Hunter† with toluylendiamin. This poison, when introduced into the circulation, gives rise to destruction of the red blood-corpuscles with liberation of hæmoglobin (hæmolysis) and to jaundice. After its administration the flow of bile is at first increased, and there is an increase in the bile-pigments poured out (polychromic), owing to an augmented amount of free hæmoglobin, the antecedent of bile-pigments, reaching the liver. After a time the amount secreted diminishes and the bile becomes more viscid, until finally the flow of bile becomes almost arrested. This slowing and diminution in the flow of bile depend on inflammation of the smaller intra-hepatic bile-ducts, which become swollen, secrete thick mucus, and are in a condition of catarrhal cholangitis due to the toxic effects of the toluylendiamin. The jaundice, therefore, is really due to obstruction, which, being situated in the small intra-hepatic ducts, is readily overlooked. This explanation accounts for the comparatively slight jaundice seen in septicæmia, pyæmia, hæmoglobinuric fever, pernicious anæmia, phosphorus and other forms of poisoning, and snake-bite. The jaundice is, therefore, toxæmic, and is dependent on changes (inflammation and obstruction) in the small intra-hepatic bile-ducts, produced by poisons in the general circulation. It may be appropriately spoken of as intra-hepatic or hæmo-hepatogenous jaundice, but not, as it formerly was, as "hæmatogenous" jaundice. Experiment shows that the presence of free hæmoglobin in the blood, though it leads to an increased secretion of bile-pigment in the bile (polychromia), does not of itself give rise to jaundice. In practice jaundice is often seen in cases where extensive hæmolysis or destruction of red blood-corpuscles is taking place. The two phenomena are the associated but independent results of infective or toxic influences which destroy the red blood-corpuscles, on the one hand, and, on the other hand, set up catarrhal inflammation of the intra-hepatic bile-ducts.

Paroxysmal hæmoglobinuria, though usually, is not necessarily, associated with jaundice. In pernicious anæmia hæmolysis in the portal area is a very marked feature, but the jaundice is slight and may be practically absent. On careful microscopic examination of the liver in pernicious anæmia catarrhal inflammation of the small bile-ducts may be seen in some instances.‡

The Question of So-called Jaundice from Polycholia.—When jaundice was found to be associated with bile in the fæces, it was supposed that there was such a profuse secretion of bile (polycholia) that an excessive amount of bile was absorbed from the mucous membrane of the intestines and bile-passages and passed through the liver into the general circulation.

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* Stadelmann: Der Icterus u. seine verscheidenen Formen, Stuttgart, 1891.

† Hunter, W.: Journ. Path. and Bacteriol., vol. iii, p. 259, 1896, and Allbutt's System, vol. iv.

‡ Compare Bret and Cade: Lyon Médical, tome xcix, p. 461.

Bile may be present in the fæces of jaundiced patients under various conditions; thus in obstruction of one hepatic duct icterus results, but the other hepatic duct pours bile into the duodenum. When a calculus lies in the common duct it may act like a ball-valve and allow bile to escape into the bowel at intervals; and in biliary cirrhosis bile is usually present in the fæces. In none of these examples is there any suggestion to the effect that an excessive secretion of bile exists. In hæmohepatogenous or toxæmic jaundice there is in the early stage a secretion of bile rich in bile-pigment (polychromia) and poor in bile acids, the pigment appearing in the excreta; obstruction in the small ducts subsequently occurs and produces jaundice. This is the explanation of so-called jaundice from polycholia. But it should be pointed out that, strictly speaking, there is not an excessive secretion of normal bile (polycholia), but only of bile-pigment (polychromia), and that the bile salts, far from being increased, are diminished.

The Question of the So-called Jaundice from Suppression of the Bile-secreting Function of the Liver.—It was formerly supposed that the liver might, from nervous or other influences, cease to secrete bile, and that an accumulation of refuse blood-pigment in the circulation resulted, which became changed, without the intervention of the liver, into bile-pigment.

Auld * has recently argued in favour of jaundice due to excessive hæmolysis, set up experimentally and regarded by him as chiefly occurring in the spleen, being independent of any bile formation in the liver, and, therefore, hæmatogenous. He found the liver cells degenerate and free from pigment, but his results are not convincing, as there was no proof that the pigment in the skin was bile.

There is no proof that in jaundice the liver does strike work, and, moreover, inasmuch as experimental research has shown that bile is only formed in the liver, jaundice could not result if the formation of bile there completely ceased. This last argument, indeed, is fatal to the idea of jaundice from suppression of the bile-forming function of the liver. In acute yellow atrophy and phosphorus poisoning the jaundice is almost certainly due to obstruction in the small intra-hepatic ducts from inflammation, and to the passage of bile into the lymphatics, which results as a natural consequence. In long-continued biliary obstruction the ducts contain clear mucous fluid devoid of bile, and it might be, and indeed has been, thought that the liver ceased to secrete bile under these conditions; but here the liver cells, as shown by the presence of bile-pigment inside them, still manufacture bile, which passes almost directly into the lymphatic vessels and so into the circulation.

"Urobilin" Jaundice.—(*Synonyms: Hæmophæic Jaundice; Acholuric Jaundice.*)—These terms have been applied to cases where the skin is yellow, but where bile-pigment is not present in the urine. It has been thought that staining of the skin indistinguishable from jaundice may be due to some pigments other than those of bile—either urobilin or a hypothetical product of hæmoglobin called hæmophein (Gubler). The reason for supposing the pigmentation of the skin to be due to urobilin was that in such cases the urine often contained an excess of urobilin. If the blood-serum in such cases, obtained from a blister or from other sources, is examined, it is found to contain bile-pigment in small quantities and not urobilin; hence the condition is one of true jaundice, and the terms "urobilin" and "hæmophœic" jaundice are erroneous and misleading. Excessive urobilinuria may occur in cases of toxæmic jaundice in which bile-pigment is temporarily absent from the urine. To this condition the term "acholuric jaundice" has been applied (Gilbert and Herscher[*]). Cases formerly called urobilin jaundice are, therefore, mild cases of jaundice in which a sufficient amount of bile-pigment passes into the circulation to stain the skin, but not enough to be present constantly in the urine. The excess of urobilin in the urine is probably due to the action of bacteria on bile-pigment in the intestine. Gilbert and Herscher, however, consider that the urobilin is manufactured by the kidneys from bile-pigment present in the blood-serum. This form of jaundice is sometimes seen in portal cirrhosis and in gastritis, and may be due to a slight secondary infection of the ducts from the duodenum (Hayem[†]). On the other hand, it may be a mild form of toxæmic jaundice. The condition is very closely allied, according to Gilbert and Herscher, to simple family cholæmia (*vide* p. 39), described by Gilbert and Lereboullet,[‡] and differs from it in the urine being more concentrated.

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* Auld: Selected Researches in Pathology, 1901.

Classification.—Jaundice may be divided, therefore, into—(1) *Extra-hepatic or "obstructive,"* where there is a gross obstruction, usually involving the large, extra-hepatic bile-ducts, to the flow of bile along the bile-ducts. (2) *Toxæmic, intra-hepatic,* or *hæmohepatogenous,* where there is obstruction in the small intra-hepatic bile-ducts. The obstruction is due to cholangitis or inflammation of the minute ducts, depending on the irritating effect of poisons derived from the blood circulating through the liver.

Jaundice is, therefore, always due to obstruction, and is a symptom, not a disease in itself. It may be the result of a purely local condition, viz., a tumor pressing on the large extra-hepatic bile-ducts; or, on the other hand, it may primarily depend on a general infective or toxæmic process which sets up angiocholitis and thus obstruction in the small intrahepatic bile-ducts.

TOXAEMIC, INTRA-HEPATIC, OR HAEMOHEPATOGENOUS JAUNDICE.

This form of jaundice, where there is no gross obstruction to the flow of bile through the larger bile-ducts, is, as has already been pointed out, obstructive and due to inflammation of the small intra-hepatic bile-ducts (angiocholitis) set up by poisons reaching the liver by the blood-stream. Hæmohepatogenous jaundice is met with in a variety of conditions which may, for convenience, be divided into two groups: (i) Various infections; (ii) as the result of certain poisons or drugs.

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[*] Gilbert and Herscher: La Presse Médicale, Dec. 27, 1902, p. 1239.

[†] Hayem: Soc. Méd. des Hôp., May 14, 1897.

[‡] Gilbert and Lereboullet: Gaz. Hebdom. de Méd. et de Chirurg., Sept. 21, 1902, p. 889.

(i) It may occur in a number of diseases, especially hæmic infections, such as pyæmia, septicæmia, relapsing fever, hæmoglobinuric fever, and may be seen in pneumonia, typhoid fever, pernicious anæmia. In some instances, as mentioned above, jaundice may occur in association with hæmolysis, for example, in paroxysmal hæmoglobinuria; the jaundice, however, is not a necessary result of hæmolysis, but a concomitant effect of a common toxic or infective cause. In the diseases enumerated above jaundice is an incidental, and in most instances not a constant, symptom of a well-recognised disease, but in some instances, as Weil's disease (or infectious jaundice) and acute yellow atrophy, it is one of the most characteristic, if not the most essential, of the clinical features.

(ii) Some of the poisons which give rise to toxæmic jaundice have been already referred to, such as toluylendiamin, phosphorus, snake-bite. In addition, jaundice occasionally follows large doses of chloroform, chloral, antifebrin (acetanilide) (P. K. Brown *), santonin, Filix mas, poisoning by arseniuretted hydrogen, anilin, mushrooms, and even in fatal cases of sulphate of copper poisoning.

General Characters and Distinctions from Obstructive Jaundice.—Hæmohepatogenous or toxæmic jaundice is essentially a sign of some underlying infection or intoxication, and is usually subordinate to the constitutional symptoms. The patient suffers comparatively little from the presence of bile in the general circulation, but is definitely and often severely ill from the primary disease or intoxication. The jaundice is, as a rule, slight, though in acute yellow atrophy and icterus gravis it is bright yellow, and the dark-green tint of chronic obstructive jaundice does not occur. There may be manifest signs of toxæmia, as shown by cutaneous, nasal, gingival, and gastro-intestinal hæmorrhages, and by nervous symptoms. The urine contains less bilirubin than in obstructive jaundice, but, owing to the fact that bile reaches the intestine and is there exposed to putrefactive and fermentative changes, urobilin is formed, absorbed, and excreted into the urine. In obstructive jaundice, where bile is excluded from the bowel, there is no urobilinuria. In both toxæmic and obstructive jaundice bile acids are present in the urine for the first few days, but not after this; the amount of the bile acids found in the urine during these early days is rather less in toxæmic than in obstructive icterus. It may be pointed out that little importance can be attached to results obtained by Pettenkoffer's well-known test, since, as employed in ordinary clinical practice, it is quite unreliable.† As the result of the general hæmic infection or intoxication there are often changes in the renal epithelium leading to albuminuria.

The fæces contain bile-pigments, sometimes even in excess; this is due to increased secretion of bile-pigments (polychromia) as a result of the toxæmia augmenting the supply of hæmoglobin to the liver cells. The motions in toxæmic jaundice thus differ markedly from the clay-coloured dejecta of cases where, from complete obstruction of the ducts, bile is excluded from the intestines.

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* P. K. Brown: American Journ. Med. Sciences, vol. cxxii, 1901, p. 770.

† Hay's sulphur test or O. F. F. Grünbaum's method of estimating bile salts should be employed.

The course of the disease is more acute, as a rule, than in obstructive icterus, and is not accompanied by the itching of the skin, xanthopsia or yellow vision, and slow pulse which may accompany obstructive jaundice. Signs of constitutional disturbance, such as enlarged spleen, fever, and albuminuria, are common, while grave symptoms develop sooner and more frequently than in obstructive jaundice, where they only occur late or at the termination of long-continued jaundice. In severe cases of hæmohepatogenous jaundice the "typhoid state," with dry tongue, delirium, coma, and multiple hæmorrhages, may rapidly develop. The important features, therefore, are the slight degree of jaundice and the presence of marked constitutional symptoms, the want of proportion between the icterus and the symptoms, and the evidence of hæmic infection or intoxication.

OBSTRUCTIVE JAUNDICE.

Signs.—*Jaundice* appears first in the conjunctiva, then successively on the face, neck, body, and extremities. The "whites" of the eyes are the first part to show the bile-pigment, but bile-pigment appears in the urine a day or two before there is any manifest jaundice. The masses of fat (pingueculæ) often seen under the conjunctiva frequently have a slightly yellow colour and may mislead a careless observer into the belief that jaundice is present. A slight degree of icterus is more readily detected in a fair-skinned patient than in one of a dark complexion, in whom the skin is often somewhat sallow. It should also be remembered that jaundice is easily overlooked in artificial light. The mucous membrane of the lips and palate shows an icteric tint, if looked for, which appears almost as soon as in the conjunctiva. When jaundice has existed for a long time, the bile-pigment in the skin turns of a dark-green colour (biliverdin), and so alters the skin that the condition is often spoken of as "black jaundice." After recovery from severe jaundice the skin is often left discoloured for a very considerable period.

In chronic jaundice, usually of some years' duration, the skin occasionally shows multiple xanthelasma. The relation between chronic icterus and this rare skin disease is not known. Xanthelasma may occur in the absence of jaundice, and it is, of course, in only a small percentage of the cases of chronic jaundice that xanthelasma develops. In chronic jaundice there is a tendency to the formation of stigmata, or spider angiomata, on the skin of the face and elsewhere. When, as the result of complete biliary obstruction or from other causes, the protective function of the liver fails, and toxines, manufactured in the alimentary canal, pass into the circulation and give rise to cholæmia or biliary toxæmia, hæmorrhages may take place into the skin and mucous membranes, giving rise to epistaxis, melæna, etc.

The urine is acid in reaction, and is somewhat diminished in amount. It becomes bile stained with bilirubin before the conjunctivæ or the skin show the icteric tint. As much as twenty-four hours may elapse between the appearance of bile in the urine and in the conjunctiva. The colour of the urine varies in different cases and at different times from an intense yellow, to brown, olive, or a very dark brown. When shaken up, the froth becomes yellow. The colour must be distinguished from that in urobilinuria, hæmaturia, melanuria, and the alterations due to rhubarb, chrysophanic acid, senna, and santonin, by Gmelin's test for bile-pigment.

Occasionally, especially in convalescence from obstructive jaundice, the urine contains no bilirubin, although the skin is still jaundiced. When bile is completely excluded from the bowel, there is no urobilin in the urine; but when the obstruction is incomplete and allows some bile to escape into the duodenum, urobilinuria may appear. This depends on the fact that urobilin is manufactured from bilirubin in the intestine as the outcome of microbic activity. Bile salts are present in the urine for the first few days of jaundice, but then disappear; the same holds good in toxæmic jaundice; but the quantity of bile salts in the urine is larger in obstructive than in toxæmic jaundice. The disappearance of bile salts from the urine probably depends on a diminished production of bile acids in all forms of icterus.

As a result of the bacterial decomposition of proteids (putrefaction) in the alimentary tract the ethereal sulphates in the urine are increased and a considerable amount of indican may be found. It must, however, be remembered that drugs like creasote and salol, which are frequently given to control flatulence, are themselves capable of increasing the amount of ethereal sulphates present in the urine.*

When, in the late stages of obstructive jaundice, a marked toxæmic condition—cholæmia—has supervened, the renal epithelium may suffer and albuminuria may occur. Casts, if carefully looked for, are almost always present; they depend on the jaundice, and are not necessarily accompanied by albuminuria.

Experimental ligature of the bile-duct has been found to give rise to casts in the urine without albuminuria. (Wallerstein.†)

The Fæces.—There is usually constipation, and the motions are often extremely offensive. In the absence of bile the fæces are pale and are devoid of urobilin; the "clay-coloured" appearance is partly due to the absence of these pigments and partly to an excess of finely divided fat and bubbles of gas. The presence of fat in excess probably interferes with absorption of proteids and favours fermentation. It has been estimated by Müller ‡ that when bile is excluded from the bowel the undigested fat may rise from 7 to 10 per cent., which is the normal, to 55 or 78.5 per cent. In exceptional cases, when obstruction is not complete, bile enters the bowel and the fæces are of a fairly normal colour and contain urobilin. This may occur when one of the two hepatic ducts is obstructed, or when a "floating" gall-stone in the common duct allows some bile to escape into the duodenum.

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* *Vide* Herter: Lectures on Chemical Pathology, p. 205.

† Wallerstein: Berlin. klin. Wochen., Bd. xxxix, S. 310, 1902.

‡ Müller: Zeitschrift f. klin. Med., Bd. xii, 1889.

Conditions of the Other Secretions.—There has been a good deal of discussion and discrepancy of opinion about the condition of the various secretions in jaundice. The majority of the secretions, such as the saliva, the mucus of the mouth and alimentary canal, are not bile-stained. The perspiration is usually free from bile, but not uncommonly bile is present in the secretions of the axilla. Tears and women's milk are more often free from bile than jaundiced. Although the bile-pigments do not appear in the saliva, the salivary glands themselves, like other organs, are deeply bile-stained. In inflammatory conditions the pathological secretions and exudations become icteric, as shown by pneumonic sputum, pleural and peritoneal effusions, and saliva in mercurial salivation.

Circulatory System.—In the absence of pain and fever the pulse tends to be slow. This is generally true, but some observers have doubted whether it is a universal rule: thus Mackenzie * has never met with a slow pulse in jaundice. It is especially in catarrhal and recent jaundice that slowing of the heart's beat is most marked. In this connexion it is interesting to note that it has been ascribed to the inhibitory action of bile salts on the cardiac ganglia; for bile acids pass into the blood in the early stage of jaundice, but are produced in very small quantities when jaundice is established. The pulse is frequently observed to vary very considerably with position; sitting up may increase the pulse-rate by twenty beats. The arterial blood pressure is low. From muscular incompetence a mitral systolic murmur may become audible, and from increased pressure in the pulmonary circulation due to this cause, or possibly to reflex constriction of the pulmonary vessels referred from the bile-ducts, the second sound over the pulmonary artery becomes accentuated.

The blood-serum is stained of a greenish-yellow tint. The specific gravity of the blood as a whole is increased, but that of the serum is unaffected. The coagulation time is prolonged, a fact of importance in conjunction with the great tendency to hæmorrhage in marked jaundice. The blood may take fifteen to twenty minutes to coagulate instead of the normal four minutes. (Osler.†) In severe cases the alkalinity of the blood has been found to be diminished.

There is very little anæmia except in severe cases; this is rather curious, inasmuch as considerable hæmolysis from the action of the bile acids might naturally have been expected. This absence of hæmolysis in jaundice is explained by the hypothesis that in jaundice the manufacture of bile acids is inhibited. In cases of advanced obstructive jaundice with cholæmia granular degeneration of the red blood-corpuscles is a prominent feature. In cholæmia there is usually leucocytosis. In jaundice of no great intensity and without grave toxæmic symptoms leucocytosis does not occur unless there is some other responsible cause, such as inflammation or suppuration.

A. S. Grünbaum,‡ in 1896, pointed out that the undiluted blood-serum of jaundiced patients in many cases agglutinated typhoid bacilli, but that when diluted, the falling-off in the agglutinative power of the serum was out of all proportion to the dilution. Eckardt * has recently drawn attention to this subject. Dr. Harold Spitta has kindly given me some unpublished observations on the relative agglutinative properties of icteric sera on the colon, Gaertner, and typhoid bacilli. In ten cases, eight of which were catarrhal jaundice, Gaertner's bacillus was not agglutinated in any; there was slight clumping of Bacillus typhosus, dilution 1 : 10, in two cases, no clumping in dilution 1 : 100. Nine cases agglutinated Bacillus coli in dilution of 1 : 10, and six cases in dilution of 1 : 100.

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* Mackenzie, J.: The Study of the Pulse, p. 134, 1902.

† Osler, W.: Johns Hopkins Hosp. Bull., vol. xii, p. 264, 1901.

‡ Grünbaum, A. S.: Lancet, 1896, vol. ii, p. 806.

The *respiration* is usually normal, but the rate may be slowed. The *temperature*, like the functions of the body generally, is depressed. This is probably due to the action of toxines on the tissues and also to the diminished intake of food and assimilation. Fever, when present, is either due to the same cause that is responsible for the jaundice, as hepatic abscess, gumma, or cirrhosis, or is the result of some complication, such as cholangitis in gall-stone obstruction.

The liver is often enlarged from damming-up of the bile, and may be tender. In malignant disease and in cirrhosis its surface may be knobby or irregular.

Enlargement of the gall-bladder is a valuable sign of obstruction of the common duct. When chronic jaundice is due to gall-stones, the gall-bladder is collapsed from previous cholecystitis, while in cases of malignant disease pressing on the common bile-duct the gall-bladder may form a tense, pear-shaped tumor. If a calculus be impacted in the cystic duct, the gall-bladder may be distended with mucus, and occasionally is enlarged from the presence of numerous calculi; there are exceptions to the general rule enunciated by Courvoisier that in jaundice due to gall-stones the gall-bladder is collapsed, while in jaundice due to malignant disease it is dilated.

The spleen is usually not enlarged, but if it is, it points to biliary cirrhosis, some septic or toxic process, such as Weil's disease or infective jaundice, to syphilis, or to that extremely rare condition, alveolar hydatid.

Symptoms.—Apart from the independent effects of underlying diseases the symptoms accompanying jaundice are due partly to the presence of bile in the circulation, which acts as a depressing poison, partly to a secondary toxæmia produced by the failure of the liver to perform its important protective function of stopping poisons brought to it from the alimentary canal, and partly to the absence of bile from the alimentary canal. These distinctions in the causation of the symptoms must not be pressed too far, but it will be convenient to consider the symptoms under the following heads:

Symptoms Due to Bile in the Circulation.—The normal constituents of bile, the bile salts, the bile-pigments, and the cholesterin, must be considered from the point of view of their toxic action on the tissues of the body.

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* Eckardt: München. med. Wochen., Bd. xlix, S. 1129.

The bile-salts exert a well-marked hæmolytic action on red blood-corpuscles outside the body, but it is plain that bile acids are not present in the blood in sufficient amounts in jaundice to produce hæmolysis. If hæmolysis due to this cause occurred, there should be marked anæmia and escape of blood-pigment in the urine in cases of obstructive jaundice. Neither of these events occurs. Anæmia may be associated with jaundice, but is not specially related to it. Hæmoglobinuria does not occur in obstructive jaundice; it is seen in some cases of toxæmic jaundice, such as hæmoglobinuric fever, and experimentally in toluylendiamin poisoning, but here the hæmolysis precedes the development of jaundice, and, like it, is due to the action of a poison. The absence of anæmia and hæmoglobinuria in obstructive jaundice and the fact that bile salts are only found in the urine during the first few days of jaundice show that the production of bile salts by the liver cells is inhibited during the existence of jaundice. The toxic effects of the bile salts are slight compared with what might naturally have been expected. The symptoms referable to the action of the bile salts are slowing of the pulse and dilatation of the peripheral vessels. The headache and mental depression may in part be due to a similar toxic effect on the brain.

Bilirubin was thought by Bouchard to be ten times more toxic than bile salts, and the comparative immunity from severe symptoms in ordinary jaundice was explained by the consideration that much of this pigment was fixed in the skin and other jaundiced tissues. It appears, however, that bilirubin is a comparatively feeble poison; the subjective symptoms which have been referred to it are xanthopsia and pruritus.

Yellow vision, or xanthopsia, has been explained as the result of the retina and media having become so infiltrated with bilirubin that the blue and violet rays are absorbed. As a result, the patient suffers from blue blindness. There is a want of relationship between the degree of jaundice and yellow vision; it may be absent in advanced icterus and present when it is but slightly marked. Yellow vision is seldom a sufficient source of annoyance to lead to a definite complaint on the patient's part, but on enquiry it is not infrequently found. It is, therefore, not an important or prominent symptom. The yellow vision which follows the administration of santonin is more noticeable.

Pruritus, or itching of the skin without any local lesion, may be due to the irritating action of the bile on the sensory endings of the nerves in the skin; on the other hand, it may appear before jaundice has begun to show itself; possibly it is then the first effect of an altered blood condition. In a case of Havilland Hall's * of carcinoma of the ampulla of Vater, itching of the skin came on a week before jaundice was detected. Such cases raise a doubt whether, after all, the itching is due entirely to the presence of bilirubin; it is possible that other concomitant poisons may give rise to it, or that the dry, ill-nourished condition of the skin is the cause. The itching is usually associated with well-developed jaundice. The irritation may be excessive and prevent sleep; the scratching may induce traumatic eczema. Urticaria and lichen are sometimes

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* Havilland Hall: Lancet, 1902, vol. i, p. 1102.

seen on a jaundiced skin. Urticaria has a very curious appearance, the bile-stained exudation making the bullæ look much more jaundiced than the surrounding skin.

Cholesterin was thought by Flint * to be the cause of the grave nervous symptoms occurring late in the course of obstructive jaundice, and the term cholesteræmia was employed in the sense that cholæmia often is now. There is no satisfactory evidence that cholesterin exerts a toxic action on the body. It is true that experimental injection of cholesterin into the body has been followed by bad results. But these were probably either mechanical and due to obstruction of small blood-vessels, or, according to Herter,† caused by the glycerin in which the cholesterin was suspended.

Symptoms Due to the Presence of Poisons Other than Bile in the Circulation.—Owing to the failure of the liver to stop poisons received from the alimentary canal, auto-intoxication results, and if the kidneys do not compensate for this by free diuresis, a toxæmic condition, analogous to that of uræmia, results. The increased fermentation and putrefactive changes consequent on the exclusion of bile from the bowel render the process of auto-intoxication one of considerable importance. In a minor degree mental depression, incapacity for continued mental effort, drowsiness, headache, and general debility are the results of this hepatic toxæmia, while in more marked degrees there may be delirium, somnolence, and coma. A bitter taste in the mouth is often complained of, although the saliva does not contain bile-pigment; this bitter flavour may depend on the presence of toxic bodies, which, owing to hepatic insufficiency, have escaped into the general circulation and passed into the saliva. There is often considerable impairment of appetite, with a special distaste for fatty food.

The tendency to hæmorrhage in chronic obstructive jaundice is a noticeable fact, and one of great importance when any surgical operation has to be performed, inasmuch as fatal hæmorrhage may result. Hæmorrhages into the skin are common, while epistaxis is sometimes a cause of great anxiety. The frequent oozing from the gums is accompanied by an offensive character of the breath. The coagulation time of the blood in chronic jaundice shows marked retardation; instead of coagulating in four minutes it may take fifteen or twenty minutes (Osler ‡). This blood change may be due to hepatic insufficiency; it may reasonably be supposed that the liver fails to stop poisons and bodies allied to peptones absorbed from the alimentary canal. The poisons would damage the walls of the blood-vessels, while the peptone-like bodies would interfere with the coagulation of the blood. It has, however, been suggested by Mayo Robson § that the hæmorrhagic tendency is pancreatic in origin, and that it may depend on a diminution of lime salts in the blood due to a profuse excretion of lime salts in the urine in pancreatitis.

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* Austin Flint, Jr.: American Journ. Med. Sciences, Oct., 1862, p. 305.

† Herter: Lectures on Chemical Pathology, p. 331.

‡ Osler, W.: Johns Hopkins Hosp. Bull., vol. xii, p. 264, Aug., 1901.

§ Mayo Robson: Brit. Med. Jour., 1901, vol. i, p. 1131, and Lancet, March 19, 1904.

The absorption into the blood of glycerin from associated fat necrosis is a possible cause of hæmorrhage, especially for local extravasation of blood in the neighbourhood of the pancreas. In two cases the blood plates were greatly diminished. (Cammidge.*)

Symptoms Due to the Absence of Bile from the Intestinal Tract.—Constipation is very common, and is usually explained as due to the absence of the natural purgative, bile. Excessive fermentation leading to flatulence and extremely offensive motions is very common. The excessive decomposition in the bowel may account for transient attacks of diarrhœa. It is probable that absorption of the poisonous bodies produced in the intestine lead to headache, mental depression, and other symptoms. The interference with the absorption of fat is an important factor and leads to considerable loss of weight. The finely diffused fat probably favours fermentative changes in the bowel in addition to interfering with absorption of the other food elements.

DIAGNOSIS OF JAUNDICE.

As has already been pointed out, jaundice may be overlooked altogether if the patient is seen only by yellow artificial light, such as gas or candle illumination. No serious difficulty should arise in distinguishing jaundice from other pigmentary changes in the skin. The yellow colour of patients with slight icterus is hardly likely to be confused with the bronzing of sunburn, with the natural hue of the yellow-skinned races of mankind, or with the tint of the skin in the advanced cachexia of malignant disease; but should any question arise, examination of the conjunctivæ and of the urine, or of blood-serum obtained from a blister, for the presence of bile-pigment will quickly settle the matter. The dark-green colour of the skin in "black" jaundice of long-continued biliary obstruction might conceivably be confused with the pigmentation of the skin in Addison's disease, hæmochromatosis, malarial melanæmia, argyria, etc., but here again examination of the conjunctivæ, urine, and blood-serum will prevent error.

The past effects of severe jaundice may give rise to some difficulty, but further investigation and the history of the case should make matters clear.

In a case reported by Cavafy † a man aged twenty-nine, who had had syphilis, had abnormal pigmentation and itching of the skin left behind by jaundice eight years previously. A committee of the Pathological Society were appointed to consider the case and reported that it was leucoderma.

Feigned Jaundice.—The skin may be coloured yellow by malingerers in order to escape active work or punishment; saffron and turmeric may be employed for this purpose.‡ The fraud should be readily detected by the absence of any bile-pigment in the conjunctivæ and urine. If an attempt is made to darken the urine by taking rhubarb or santonin,

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* Cammidge, P. J.: Quoted by Mayo Robson.

† Cavafy, J.: Trans. Path. Soc., vol. xxxii, p. 258.

‡ Wickham Legg: Jaundice, etc., p. 375.

Gmelin's reaction with nitric acid is absent, and the addition of alkalis turns the urine red instead of brown.

DIFFERENTIAL DIAGNOSIS OF JAUNDICE DUE TO VARIOUS CAUSES.

Since the distinction between obstructive jaundice and toxæmic (or hæmohepatogenous) jaundice has already been considered (p. 531), it is now only necessary to refer to the differential diagnosis and the various causes of obstructive jaundice. The causes of obstructive jaundice are very numerous, but for convenience they may be grouped into three classes:

(1) Where the obstruction is inside the lumen of the bile-ducts, such as a gall-stone or parasites. (2) Where the obstruction depends on changes originating in the walls of the larger bile-ducts, *e. g.*, catarrhal cholangitis. (3) Where obstruction is produced by processes arising outside the larger ducts. Thus tumors or adhesions may mechanically compress the ducts. Malignant tumors may either merely compress or may actually invade the ducts; the former is more frequent.

I. Jaundice Due to Obstruction Inside the Lumen of the Duct.— These causes of obstructive jaundice are considered elsewhere. (*a*) Gallstones are described on page 703. It is possible that inspissated mucus may obstruct the ducts, but the cause of the excessive amount of mucus is inflammation of the ducts and gall-bladder and need not be separately described here. Inflammation of the minute intra-hepatic ducts occurs in toxæmic jaundice, in biliary cirrhosis (p. 306), and possibly in simple family cholæmia (*vide* p. 39).

(*b*) *Parasites* may gain access to the ducts and mechanically occlude the lumen. A hydatid cyst may discharge into the ducts, and, as a result, pieces of membrane or daughter cysts may block the ducts and give rise to biliary colic, jaundice, and often to infective cholangitis. The diagnosis depends on the history that the patient has either had a cyst which has disappeared, or that an existing one has grown smaller about the time that the symptoms appeared; or, still better, on the presence of bile-stained pieces of hydatid membrane in the fæces or possibly even in the vomit. The subject is considered more at length on page 415.

Round-worms (Ascaris lumbricoides) may enter the common bileducts from the duodenum and give rise to jaundice. Of this rare condition Mertens * has collected 48 examples. Distomum hepaticum, the liver fluke so fatal to sheep, has been found in the ducts of the human liver, as have, in rare instances, Distomum sinense and Distomum conjunctivum. In these cases the diagnosis depends on the recognition of the worms or their ova in the fæces. Reference is made to this subject in the section on Parasitic Affections of the Bile-ducts (p. 677).

(*c*) As pathological curiosities some authors have referred to the presence of *foreign bodies*, such as fruit-seeds, small cherry-stones, and needles, in the bile-ducts (Graham †), but suspicion as to the nature of such foreign bodies must always arise unless the absence of the constituents of gall-stones has been definitely proved.

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* Mertens: Deutsch. med. Wochen., Bd. xxiv, S. 358, 1898.

† Graham, J. E.: Loomis and Thompson's System of Medicine, vol. iii, p. 428.

(*d*) In most exceptional instances *new growth* may extend along the lumen of the common bile-duct and occlude it without necessarily invading the walls of the duct except at the point where it originates or gains entrance into the lumen of the duct. This has been observed in primary malignant disease of the gall-bladder—a cylinder of growth projecting into the common bile-duct (Bohnstedt*)—and in primary carcinoma of the liver. (Gilbert and Claude.†)

II. **Jaundice Due to Changes in the Walls of the Larger Ducts.**—(*a*) *Catarrhal jaundice* due to inflammatory swelling of the mucous membrane of the common bile-duct, either inside the biliary papilla or in the lower part of the duct, is described elsewhere (p. 655) under the heading of Acute Catarrhal Cholangitis. It is due to the spread of inflammation from the duodenum, and is preceded by gastro-intestinal disturbance—vomiting and diarrhœa. It is usually of short duration, and is not accompanied by the fever, enlarged spleen, albuminuria, and jaundice seen in infectious jaundice.

(*b*) *The infective and suppurative forms of cholangitis* are usually associated with gall-stones or the rupture of an hydatid cyst into the ducts, but comparatively often complicate the rare condition of malignant disease of the duodenum involving the papilla. Infective cholangitis presents the symptoms of intermittent hepatic fever (*vide* p. 750), while in suppurative cholangitis (*vide* p. 663), where, however, jaundice is by no means constant, the clinical picture is that of intra-hepatic suppuration and may closely resemble suppurative pylephlebitis. It may be pointed out that jaundice in the roseolous stage of syphilis may possibly be due to a specific change, resembling the cutaneous rash, in the bile-ducts. (*Vide* p. 348.)

(*c*) *Simple stricture* of the large bile-ducts may be congenital (*vide* p. 639, Congenital Obliteration of the Ducts) or acquired, and due to cicatrization of an ulcer in the ducts. Apart from the cystic duct, stricture of which does not give rise to jaundice, simple stricture of the ducts, such as might conceivably follow cicatrization of an ulcer set up by a gall-stone, is extremely rare. Hence in practice cases of jaundice following biliary colic should be regarded as due either to fresh gall-stone impaction or to malignant disease. Simple stricture of the ducts is described on page 653.

(*d*) *Primary growths of the ducts* may be carcinomatous, or in rare instances innocent; the malignant growths (*vide* p. 683) occlude the lumen and give rise to deep, progressive jaundice and usually to enlargement of the gall-bladder. At first, since there is often colic, it may resemble cholelithiasis, except for the dilated gall-bladder, while later it resembles malignant disease of the head of the pancreas. Innocent tumors, such as papillomata, are really curiosities (*vide* p. 681). Xanthelasma has been described as arising in the mucous membrane of the ducts and causing jaundice, but there is some reason to doubt whether this is the true interpretation of these cases.

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* Bohnstedt, quoted by Devic and Gallavardin: Rev. de Méd., July, 1901, p. 569.

† Gilbert and Claude: Archiv. général. de Méd., 1895, clxxv, p. 53.

(*e*) *Spasm* of the muscular coats of the ducts seems to be a very reasonable explanation of *emotional jaundice,* but it has not received much support. It also explains jaundice in hysterical subjects when there is no evidence of catarrh or other causal factor. The occurrence of jaundice in cases of lead poisoning might, in the absence of any other satisfactory cause, be referred to spasm of the ducts. I have seen recurrent attacks of painful jaundice in a worker in lead which did not appear to be due to gall-stones.

III. **Jaundice Due to Pressure Exerted on the Bile-ducts from Without.**—*Synopsis.*—1. By intrahepatic tumors.

2. By enlarged glands in the portal fissure—
    Gummata, malignant, tuberculous, syphilitic.
3. In lesions of the stomach—
    Carcinoma.
    Gastric ulcer; perigastric adhesions.
4. In duodenal lesions—
    Ulcer.
    Carcinoma.
5. By peritoneal adhesions.
6. By renal and suprarenal tumors—
    In nephroptosis.
7. By retroperitoneal tumors.
8. In pancreatic lesions—
    Carcinoma. Cysts. Chronic pancreatitis. Gumma.
9. By aneurysm of the aorta, hepatic, mesenteric arteries.
10. In gastroptosis.
11. In hepatoptosis.
12. By uterine and ovarian tumors. Pregnant uterus.
13. Constipation.

(1) *Intrahepatic Tumors, etc.*—Tumors inside the liver, such as carcinoma, may press on the intrahepatic branches of the bile-ducts, and if the obstructed area is a large one, such an amount of bile stasis may result as to lead to absorption of bile by the lymphatics and so to jaundice. In these cases bile may pass from the other lobe of the liver into the duodenum, so that the fæces retain their normal colour. A hydatid cyst or a gumma in the liver may act in a similar fashion.

Primary or secondary malignant disease of the liver may project into the portal fissure and press upon the hepatic ducts, the common hepatic or common bile-ducts, and so give rise to jaundice. Hydatid cysts or gummata, when projecting from the liver, may exert pressure on the bile-ducts in a similar manner.

In a case recorded by Legg * a hydatid cyst projecting from the liver compressed the common hepatic duct and gave rise to persistent jaundice with xanthelasma multiplex. Bristowe † described obstruction of both hepatic ducts by gummata.

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* Legg, J. W.: Trans. Path. Soc., vol. xxv, p. 155.

† Bristowe, J. S.: Trans. Path. Soc., vol. ix, p. 233

(2) *Enlargement of the glands in the portal fissure* may be due to various causes, such as intra-hepatic inflammation, malignant disease, and occasionally to tubercle and syphilis. Malignant infiltration of the glands, which is the most frequent cause of jaundice, may be secondary to disease in the liver, gall-bladder, stomach, pancreas, intestine, or peritoneum.

Tuberculous glands in the portal fissure may in rare cases press on the bile-ducts and give rise to obstructive jaundice. Cases have been recorded by Florand,[*] Kester,[†] Knight,[‡] Hodenpyl.[§] The rarity of tuberculous disease of the glands in the portal fissure depends on the fact that they receive the lymphatics from the liver, and not from the intestine and peritoneum. Tuberculous enteritis and peritonitis, therefore, give rise to tuberculous enlargement of the portal glands in a roundabout manner, viz., by producing tuberculous infection of the portal spaces in the liver—the bacilli travelling by the portal vein. The lymphatics of the liver then become involved and convey the infection to the portal glands. It is conceivable that tuberculous infection might extend along the lymphatic trunks against the flow of lymph and so spread to the portal fissure from the abdominal cavity. Tuberculous enlargement of the portal glands is, therefore, closely bound up with tuberculosis of the liver (*vide* p. 336), in which, however, jaundice is most exceptional. A tuberculous gland in the portal fissure has been known to open into the common bile-duct (Kester), much in the same way that tuberculous bronchial glands have been found to open into the trachea. Tuberculous glands may become adherent to the structures in the portal fissure and render any attempt at removal both difficult and dangerous. In Florand's case removal of tuberculous glands compressing the common bile-duct was followed by fatal hæmorrhage from the portal vein.

Tuberculous retroperitoneal lymphatic glands may compress the common bile-duct near its entrance into the duodenum and give rise to obstructive jaundice. The glands may so indent the pancreas as to look at first like tuberculosis of that organ.

Syphilitic Adenitis.—It has been tentatively suggested that enlargement of the glands in the portal fissure may be the cause of the specific jaundice seen in rare instances at the same time as the roseola in syphilis, but this is extremely doubtful. It is possible that gummatous change or syphilitic adenitis later in the course of the disease may involve lymphatic glands in the neighbourhood of the bile-ducts, and, by pressure, give rise to obstructive jaundice. This condition is closely allied to gummatous infiltration about the head of the pancreas (*vide* p. 549).

A man aged thirty-two years was under my care with chronic jaundice; as he did not improve, an exploratory operation was done by Mr. A. M. Sheild, and some hard masses were felt along the course of the common bile-duct. Although there was no manifest evidence of syphilis, he was put on iodides and mercury and became completely cured. The absence of any roseola, or, indeed, of any history of syphilis, made it unlikely that this case was one of jaundice in the early stages of syphilis (*vide* p. 348), and it may have been due to gummatous adenitis.

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[*] Florand: La Semaine Médicale, 1899, p. 20.
[†] Kester: Centralblatt f. inn. Med., 1896, S. 213.
[‡] Knight: Quarterly Med. Journ. (Sheffield), July, 1895.
[§] Hodenpyl: Medical Record (N. Y.), Nov. 12, 1898.

A *gumma in the portal fissure* may press on or involve the bile-ducts and so give rise to jaundice.

S. West[*] recorded a remarkable example of a large gumma extending from the diaphragm to the neck of the gall-bladder, measuring 4½ × 2½ inches. The patient, a girl aged fifteen years with jaundice, was the subject of congenital syphilis.

Cases of tardive hereditary syphilis with jaundice and due to constriction of the bile-ducts by dense adhesions have been put on record by Mackenzie[†] and Lazarus-Barlow.[‡]

(3) *Lesions of the Stomach.*—Jaundice occurs in from 6 to 13 per cent. of all cases of *gastric carcinoma.* It occurs more often in cases where the lesser curvature and the pylorus are affected, and is less frequent when the cardiac end of the stomach is involved.

Jaundice was present in 4 per cent. of Osler and Macrae's[§] cases, in 5.5 per cent. of Brinton's[‖] cases, and in 13.7 per cent. of Fenwick's.[**]

Usually jaundice is due to pressure exerted by enlarged lymphatic glands on the ducts, either in the portal fissure or close to the head of the pancreas. In some cases of carcinoma of the pylorus or of the lesser curvature of the stomach the growth spreads by direct continuity into the lesser omentum and may thus surround the common bile-duct and compress and invade its walls.

This was well shown in a remarkable case of spheroidal-celled carcinoma of the pylorus in a boy aged sixteen years who died in St. George's Hospital with marked jaundice.

It is noteworthy that in secondary malignant disease of the liver jaundice is more frequent when the primary growth is in the stomach than when it is in some more distant part of the abdomen, such as the rectum. This depends on the fact that jaundice is less often due to the actual metastasis in the liver itself than to glandular infection in the immediate neighbourhood of the ducts or to the direct spread of growth into the lesser omentum.

In Gastric Ulcer and Perigastritis.—Jaundice due to the spread of inflammatory adhesions from a gastric ulcer near the pylorus must be a very rare event, as it is not mentioned by Murchison, Habershon, Brinton, or by Dreschfeld.[††]

That it may occur is shown by the following case.[‡‡]

A man aged twenty-seven came under my care in St. George's Hospital with no definite history whatever of gastric ulcer, but with dyspepsia and occasional vomiting of six weeks' duration and jaundice of two weeks' standing. The stomach was dilated and a definite pyloric tumor with what was thought to be thickening of the adjacent curvatures was palpable. The case was regarded as carcinoma of the pylorus, but as unsuitable for gastrojejunostomy. At the postmortem there was no malignant disease, but a cicatrising ulcer at the pylorus giving rise to marked narrowing of that orifice and extensive peripyloric adhesions involving the common duct. The head of the pancreas, which was enlarged from chronic interstitial pancreatitis, had been felt in life and regarded as thickening of the curvatures of the stomach near the pylorus.

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[*] West, S.: Trans. Path. Soc., vol. xli, p. 155.

[†] Mackenzie, H. W. G.: Ibid., vol. xliii, p. 84.

[‡] Lazarus-Barlow, W. S.: Ibid., vol. l, p. 158.

[§] Osler and Macrae: Cancer of the Stomach, p. 55, 1900.

[‖] Brinton: Diseases of the Stomach, p. 211, 1864.

[**] Fenwick, S.: Cancer and Tumors of the Stomach, p. 69, 1902.

[††] Dreschfeld, J.: Allbutt's System of Medicine, vol. iii.

[‡‡] Rolleston: Practitioner, Nov., 1897.

A case of jaundice and ascites in a man aged thirty-nine years due to fibrosis spreading from an ulcer near the pylorus to the portal fissure is recorded by James.[*] The common bile-duct was normal, but the two hepatic ducts were compressed by cicatricial tissue which spread into the liver along the portal spaces.

The converse condition, viz., pericholecystitic adhesions producing pyloric obstruction, has been fully recognised and is much less rare.

(4) *Duodenal Lesions.—Duodenal ulcer* may in very rare instances be associated with jaundice either (i) as a complication or (ii) as an after-result.

(i) Ulceration of the duodenum is almost always limited to the first part of the duodenum and hardly ever extends sufficiently far into the second part to invade the biliary papilla. Concomitant duodenal catarrh, however, may spread to the biliary papilla.

Perry and Shaw [†] record several cases of duodenal ulcer with jaundice. Murchison [‡] describes a case in a man aged sixty-nine, but there is a strong suspicion that there was malignant disease of the duodenum in the region of the biliary papilla.

(ii) As a sequela from the results of cicatrization and healing of the ulcer. If, as rarely happens, the ulcer is in the second portion of the duodenum and involves the papilla, cicatricial contraction may give rise to permanent obstructive jaundice.

Budd [§] described a case of this kind, and Perry and Shaw [‖] refer to 4 cases examined after death where a cicatrised duodenal ulcer obstructed the outflow of bile from the biliary papilla. Zoia [**] records cicatrisation of a duodenal ulcer obstructing the bile and pancreatic ducts and imitating carcinoma of the head of the pancreas.

Inflammatory adhesions may spread out from a duodenal ulcer in the first part and compress the common bile-duct as it runs towards the biliary papilla. This mechanism is exactly like that already described in peripyloric adhesions.

Morgan [††] has recorded the details of a case in which the common bile-duct was firmly bound to the base of a duodenal ulcer by dense adhesions and its lumen much constricted. The patient, a man aged fifty-two years, died deeply jaundiced.

Carcinoma of the duodenum is not a common disease, and need not cause any interference with the outflow of bile unless the growth is situated in the second part of the duodenum and involves the biliary papilla by extension or actually starts in the intestinal mucous membrane of the biliary papilla. This latter form of duodenal carcinoma—juxta-ampullary or perivaterian, as it is sometimes called—imitates cancer of the head of the pancreas, and, like it, should present the sign of Bard and Pic, viz., deep jaundice and distension of the gall-bladder, but in addition it has a special tendency to set up infective cholangitis, multiple foci of suppuration in the liver, and fever. Specimens of this condition are to be found in the museums of St. Bartholomew's, Guy's, and St. Thomas' Hospitals. The following case illustrates this sequence of events:

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[*] James: Scottish Medical and Surgical Journal, vol. ii, p. 511.

[†] Perry and Shaw: Guy's Hosp. Reports, vol. l, 1893.

[‡] Murchison: Diseases of the Liver, p. 422, 3d ed., 1885.

[§] Budd: Diseases of the Liver, p. 204, 1857.

[‖] Perry and Shaw: Guy's Hospital Reports, vol. l, p. 273, 1893.

[**] Zoia: Gaz. med. di Torino, May 11, 1899.

[††] Morgan, J. H.: Trans. Path. Soc., vol. xxvii, p. 176

Carcinoma of Biliary Papilla, Jaundice, Suppurative Cholangitis, Secondary Abscesses in Prostate and Kidneys.—A man aged fifty-two years was under the care of my colleague, Sir Isambard Owen, in St. George's Hospital with jaundice of ten months' duration, which, however, had disappeared for one month during this period of ten months, loss of strength and flesh, and difficulty in passing water. The liver was much enlarged, but not tender; there was no ascites. The urine contained bile and an excess of ethereal sulphates and indican. There were pus in the urine, a greatly enlarged prostate, and some diarrhœa. There was a hectic temperature during the last five weeks of life. The tentative diagnosis was malignant disease of the prostate with a secondary growth in the portal fissure producing jaundice. At the autopsy there was a carcinomatous growth involving the duodenal surface of the biliary papilla, with great dilatation of the common and of all the bile-ducts in the liver; there were universal suppurative cholangitis and empyema of the gall-bladder. The liver was green, not fibrosed, and contained some secondary nodules of white growth. The pancreatic duct was dilated. The enlargement of the prostate was due to an abscess; there were numerous abscesses in the two kidneys.

Cases of perivaterian carcinoma of the duodenum without marked jaundice have been recorded by Lannois and Courmont[*] and by Descos and Bériel.[†]

Carcinoma of the duodenum may give rise to jaundice in another way, viz., by inducing gastroptosis, which, if there are adhesions around the ducts, may induce kinking and jaundice. (*Vide* Gastroptosis, p. 550.)

Mackie Whyte[‡] has put a case on record where cancer of the duodenum, not involving the biliary papilla, led to great distension of the stomach and so to kinking of the common bile-duct and jaundice.

(5) *Peritoneal adhesions* around the hepatic or common bile-ducts may produce kinking of the ducts and thus lead to jaundice. Such adhesions may be due to local peritonitis set up in various ways, such as by gall-stones in the gall-bladder, perigastric inflammation (p. 543), adhesions around a duodenal ulcer (p. 544), adhesions to inflamed retroperitoneal glands (B. Robinson[§]), or possibly by adhesions due to perihepatitis (S. Phillips[‖]). It is, however, remarkable how seldom perihepatitis and chronic peritonitis are accompanied by jaundice.

(6) *New-growths of the right kidney or suprarenal* body very seldom press on the bile-duct and so directly produce jaundice, but secondary growths in the portal fissure may set up jaundice.

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[*] Lannois and Courmont: Rev. de Méd., 1894, p. 291.

[†] Descos and Bériel: Rev. de Méd., 1899, p. 633.

[‡] Whyte, M.: Scottish Med. and Surg. Journ., vol. i, p. 361, 1897.

[§] Byron Robinson: American Med. and Surg. Bulletin, April, 1896.

[‖] Phillips, S.: Lancet, 1903, vol. i, p. 1796.

In 26 cases of primary malignant disease of the suprarenal bodies jaundice was not present in any. (Rolleston and Marks.[*])

That *a floating kidney* can exert direct pressure on the bile-ducts and thus lead to jaundice, as suggested by Litten[†] and others, is regarded as improbable by Macalister.[‡] The colic, jaundice, and vomiting induced by a floating kidney on the right side may be explained in the following way: the peritoneum over the kidney being continuous with that covering the duodenum and common bile-duct, undue mobility of the kidney will exert traction on the duodenum and common bile-duct and will lead to narrowing of the bile-duct and duodenum. It has been pointed out that nephroptosis may also lead to downward displacement of the duodenum, with stretching of the common bile-duct, displacement of the gall-bladder, with sharp kinking of the cystic duct, torsion of the vertical part of the duodenum, and perhaps even of the bile-duct. (J. Hutchinson, Jr.[§])

A floating kidney may not only produce symptoms exactly like hepatic colic and induce jaundice, but the displaced kidney may readily be mistaken for a distended gall-bladder. Hutchinson has described two cases where what was thought to be the gall-bladder turned out to be a floating right kidney.

Cases of jaundice diagnosed as cholelithiasis and shown to be due to floating kidneys have been recorded by Maclagan and Treves (3),[‖] by Hale White,[**] Cordier,[††] Fenwick,[‡‡] Lawrie.[§§]

The diagnosis depends on the detection of a floating kidney, for the symptoms, biliary colic and jaundice, are the same as those of cholelithiasis. If the symptoms persist after the floating kidney has been efficiently and successfully treated, it is probable that there is cholelithiasis in addition.

(7) *Pressure Exerted by Retroperitoneal Tumors.*—In rare instances retroperitoneal tumors have been known to give rise to jaundice by pressure on the common bile-duct.

Vander Veer[‖‖] recorded a large retroperitoneal myxosarcoma (weight 6 pounds) arising from the region of the left adrenal body, which so interfered with the bile-duct as to produce jaundice.

A hydatid cyst arising in connexion with the retroperitoneal space near the head of the pancreas may compress the common duct. This is illustrated by a specimen (No. 2256) in St. Bartholomew's Hospital Museum.

(8) *Lesions of the Pancreas Producing Jaundice.*—Malignant disease,

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[*] Rolleston and Marks: American Journ. Med. Sciences, vol. cxvi, p. 398, Oct., 1898.

[†] Litten: Berlin. Charité-Annalen, 1880, S. 10.

[‡] Macalister, A.: Allbutt's System of Medicine, vol. iv, p. 346.

[§] Hutchinson, J., Jr.: The Practitioner, 1902, vol. lxviii, p. 186.

[‖] Maclagan and Treves: Lancet, 1900, vol. i, p. 15.

[**] Hale White: Brit. Med. Journ., 1892, vol. i, p. 223.

[††] Cordier: American Journ. of Obstet., 1896, vol. xxxiv, p. 532.

[‡‡] Fenwick: Lancet, 1899, vol. ii, p. 1296.

[§§] Lawrie: Brit. Med. Journ., 1901, vol. i, p. 15.

[‖‖] Vander Veer: American Journ. of the Medical Sciences, vol. ciii, p. 22, Jan., 1892.

cysts, chronic interstitial inflammation, gummata, and calculi in Wirsung's duct are all capable of compressing the common bile-duct and producing obstructive jaundice, but with the exception of the first named are rarely recognised as acting in this manner.

Malignant disease of the pancreas may be primary or secondary, but it is almost entirely with primary malignant disease that we are at present concerned. It is practically always carcinoma, and usually attacks the head of the gland—according to Hale White,* in 85 per cent. of the cases. When in this situation, the growth readily compresses the common bile-duct near its termination, but when the growth is limited to the tail or body of the pancreas, jaundice does not result unless a secondary growth compresses the duct or there is some other cause for jaundice, such as a calculus in the common duct. Jaundice is met in a majority of cases of primary malignant disease of the pancreas.

Mirallié † found it in 82 out of 113 cases, but Hale White gives a lower estimate, viz., in "probably more than half the cases," and considers that the incidence of icterus has been somewhat exaggerated by previous writers. Oser gives two-thirds as the proportion of cases in which jaundice occurs.

The jaundice may come on gradually and painlessly, or be accompanied by colic. It is permanent and progressive, and becomes intense, so that cholæmia develops comparatively early. The other distinctive features of malignant disease of the head of the pancreas are rapid and extensive wasting, the presence of a tumor in the position of the pancreas, which, however, is only palpable in a small minority of the cases, and distension of the gall-bladder. The association of deep jaundice with a large gall-bladder was specially insisted upon by Bard and Pic,‡ and is sometimes spoken of as the sign of Bard and Pic. It illustrates Courvoisier's law, which is to the effect that biliary obstruction due to new-growth is accompanied by an enlarged gall-bladder, while in gall-stone obstruction of the common duct the gall-bladder is small. As a matter of fact, however, the gall-bladder, even though enlarged as shown by postmortem examination, is not always palpable during life. As already pointed out, the diagnosis depends on the intense jaundice, the rapid loss of weight, and the enlargement of the gall-bladder. It is, however, practically impossible to distinguish it from primary carcinoma of the common bile-duct.§ In primary carcinoma of the ampulla of Vater (*vide* p. 697) and of the duodenal surface of the biliary papilla the jaundice may intermit, which it never does in malignant disease of the pancreas, and fever from infective cholangitis may supervene. From a calculus in the common duct the diagnosis may be easy when the cases are typical, but sometimes it is difficult, as attacks of pseudo-biliary colic may occur about the time of the onset of jaundice in malignant disease of the pancreas, while pain may be absent in some cases of calculus in the common duct. The history of the cases and the course of the disease, especially the character of the jaundice, progressive or intermittent, and the condition of general nutrition will usually clear up a diagnosis which at first was doubtful.

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* Hale White: Guy's Hosp. Reports, vol. liv, p. 17.

† Mirallié: Gaz. des Hôp., 1893, p. 889.

‡ Bard and Pic: Rev. de Méd., vol. viii, p. 257.

§ Cammidge's test, however, provides a means of distinguishing between these two conditions.

Cammidge's Test.—By treating the urines, free from sugar, of cases of pancreatic disease by a special method, which cannot be described further here except to state that the urine is first boiled with HCl and then with sodium acetate and phenyl-hydrazin hydrochlorate, Cammidge[*] obtained crystals which could not be got from normal urine. He was further able to differentiate between the crystals obtained from the urine of (i) malignant disease, (ii) acute inflammation, and (iii) chronic inflammation of the pancreas. Jaundice due to pancreatic disease could thus be distinguished from jaundice due to other causes, and further malignant disease could be diagnosed from inflammatory affections of the pancreas. These results have been freely criticised, and, though they appear valid, the subject is still open for discussion.

Malignant disease of the pancreas may be associated with cholelithiasis, and in rare instances with gall-stones in the common duct.

Thus a woman aged fifty-eight, under my care in St. George's Hospital in September, 1899, was thought to be suffering from gall-stone obstruction and was accordingly operated upon; a gall-stone was felt, and on manipulation was displaced, it was thought, into the duodenum. Death occurred on the third day, largely from hæmorrhage at the site of operation. At the autopsy it was found that the calculus had been pushed back into the gall-bladder, and that all the ducts were greatly dilated. The gall-bladder was small and contained two round large cholesterine calculi. The head of the pancreas contained a colloid carcinoma which did not involve the duct, so the jaundice was probably due to the stone in the common duct. Microscopically the growth was a spheroidal-celled carcinoma undergoing extensive colloid change.

Pancreatic Cysts, etc.—Jaundice is rarely due to a pancreatic cyst, but may occur when the cyst is situated sufficiently close to the bile-duct to compress it. Pancreatic and peripancreatic cysts may present in various situations: (1) Above the stomach and below the liver (interhepatico-gastric type). (ii) Between the greater curvature of the stomach and the transverse colon; this is the commonest form (subhepatico-gastric type). (iii) Below the transverse colon, so that the cyst projects near the umbilicus (subhepato-gastro-colic type).

Cysts which pass forwards between the stomach and the transverse colon (subhepatico-gastric type) may compress the common bile-duct. Oser[†] has collected 15 cases in which jaundice has occurred.

A man aged thirty with jaundice of three months' duration under my care in St. George's Hospital was operated upon by Mr. G. R. Turner and a pancreatic cyst found projecting between the greater curvature of the stomach and the transverse colon.[‡] After drainage the jaundice disappeared and the man recovered. Turney and Ballance[§] met with a case of jaundice in a man aged thirty-five in whom the symptoms were thought to point to calculous obstruction of the common bile-duct; laparotomy, however, proved that the jaundice was due to the pressure of a pancreatic cyst. Cases have also been described by Havilland Hall,[‖] McPhedran.[**]

A hydatid cyst in the pancreas is a pathological curiosity.

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[*] Lancet, March 19, 1904.

[†] Oser: Nothnagel's Encyclopædia of Practical Medicine, p. 195, English Translation.

[‡] *Vide* also Trans. Medical Soc., vol. xxi, p. 94.

[§] Turney and Ballance: St. Thomas' Hospital Reports, vol. xxvi.

[‖] Havilland Hall: Trans. Medical Soc., vol. xxi, p. 107.

[**] McPhedran: Trans. Associat. American Physicians, vol. xii, p. 61.

A hydatid cyst in the head of the pancreas was the cause of jaundice of ten months' duration and of ascites in a boy aged six years. At the autopsy the gall-bladder was dilated and the bile-duct and portal vein were stretched over the cyst and so compressed that it was impossible to force bile from the distended gall-bladder into the duodenum before the cyst was opened. The liver was enlarged, granular on the surface, and fibrosed.*

Chronic Interstitial Pancreatitis.—Mayo Robson † and Barling ‡ have drawn attention to the fact that chronic inflammation of the head of the pancreas may compress the common bile-duct and produce a train of symptoms—obstructive jaundice, colic, and wasting—strongly suggesting malignant disease or impacted gall-stones. This chronic fibrosis may be directly due to gall-stones in the common duct and may persist after the stone is expelled. The diagnosis of these cases is very difficult, and the moral drawn from them is that it is advisable to admit such cases to operation. In some instances the gall-bladder has been drained, either externally or into the small intestine, while in other cases the abdomen has been closed without any more radical measure than manipulation of the parts. Recovery has followed both of these methods of surgical treatment. It is possible that where the parts have merely been manipulated (Owen,§ Dalziel ‖) a calculus in the orifice of the biliary papilla may have been displaced into the duodenum. It seems highly probable that cases of chronic interstitial pancreatitis have been regarded not only during life, but even after death, as examples of carcinoma of the head of the pancreas. According to Hale White,** however, chronic interstitial pancreatitis is a rare disease; for in forty-one years there were 19,000 necropsies at Guy's Hospital with only four cases of this disease.

In cases of pancreatitis the secretion of the gland escapes into the surrounding tissues and sets up fat necrosis. As a result of this glycerine and fatty acids are liberated. It was first thought that the tendency to hæmorrhage, both in acute inflammation of the pancreas and in cases of chronic pancreatitis, which is so often accompanied by chronic jaundice, might be due to the action of glycerine (Mayo Robson ††), but more recently Mayo Robson ‡‡ refers it to a diminution of the lime salts in the blood depending on increased excretion of lime in the form of oxalates in the urine.

Closely allied to chronic interstitial pancreatitis is the extremely rare condition gummatous infiltration in and around the head of the pancreas.

In a man aged thirty-three who had had syphilis ten years previously, and was suffering from marked obstructive jaundice H. B. Robinson §§ opened the abdomen, felt a growth in the situation of the head of the pancreas, and accordingly put the gall-bladder into communication with the hepatic flexure of the colon. Under iodide of potassium the mass disappeared and there was a gain in weight of two stones. A similar case of Da Costa's is mentioned in Gould's Year-book of Surgery for 1902, p. 181. Moynihan[*] has also described this condition.

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* Guy's Hospital Museum, No. 1475.

† Mayo Robson: Brit. Med. Journ., 1900, vol. ii, Epitome, p. 26. Lancet, 1900 vol. ii.

‡ Barling: Brit. Med. Journ., 1900, vol. ii, p. 1766.

§ Owen: Brit. Med. Journ., 1902, vol. ii, p. 1311, and Hale White: Brit. Med. Journal, 1903, vol. ii, p. 126.

‖ Dalziel: Brit. Med. Journ., 1902, vol. ii, p. 1312.

** Hale White: Brit. Med. Journ., 1903, vol. ii, p. 126.

†† Mayo Robson: Philadelphia Medical Journal, June 1, 1901.

‡‡ Lancet, 1904, vol. i, March 7.

§§ Robinson, H. B.: Brit. Med. Journ., 1900, vol. ii, p. 1004.

A large pancreatic calculus in the termination of Wirsung's duct may compress the end of the common bile-duct and give rise to jaundice.

Pearce Gould[†] has recorded a case where a pancreatic calculus the size of a horse-bean gave rise to jaundice.

(9) *Aneurysms of the Abdominal Aorta, etc.*—An aneurysm of the abdominal aorta near the cœliac axis may exert pressure on the common bile-duct and so give rise to jaundice and dilatation of the gall-bladder. Cases have been recorded by Stokes[‡] and W. L. Dickinson.[§]

In a man aged twenty-eight, who had syphilis when twenty years of age, a sacculated aneurysm involving the origin of the cœliac axis burst into the second part of the duodenum a short distance above the biliary papilla. The common bile-duct was compressed and the gall-bladder distended. Jaundice occurred three days before death, which was preceded by sudden and profuse hæmatemesis. (W. L. Dickinson.)

Aneurysms of the hepatic artery are rare, but when they do occur, are frequently accompanied by jaundice. The aneurysm may compress the bile-ducts above the entrance of the cystic duct, and hence the gall-bladder need not be dilated, as in jaundice due to an aortic aneurysm. An aneurysm of the hepatic artery may, by interfering with the blood-supply to the bile-ducts, dispose to infection, cholangitis, and thus give rise to suppuration in the ducts. (*Vide* p. 44.)

An *aneurysm of the superior mesenteric artery* near its origin from the aorta has been known to compress the bile-duct and give rise to jaundice. Cases have been published by Dr. J. A. Wilson[‖] and Sir W. T. Gairdner.[**] The majority of aneurysms on this vessel, however, are not associated with jaundice. Those on the peripheral portions of the artery or its branches are not in relation with the bile-ducts, and therefore do not compress them.

(10) *Gastroptosis* is not infrequent, but its association with jaundice is rare. Steele[††] states that gastroptosis alone cannot produce sufficient pressure on the bile-ducts to obstruct the flow of bile along the ducts; this is based on his observations that after death downward displacement of the pylorus, so as to imitate the conditions present in gastroptosis, though it stretched the gastrohepatic omentum, did not interfere with the passage of bile into the duodenum: If, however, there were any adhesions involving the ducts in the portal fissure, a very moderate amount of displacement of the pylorus produced kinking of the ducts and obstruction. It would thus appear that if there are any adhesions around the ducts, gastroptosis will readily produce jaundice.

(11) *Hepatoptosis.*—In wandering liver jaundice may be due to the

[*] Moynihan: Lancet, 1902, vol. ii, p. 856.
[†] Gould, A. P.: Trans. Clin. Soc., vol. xxxii, p. 59.
[‡] Stokes: Diseases of Heart and Aorta, 1854, p. 633.
[§] Dickinson, W. L.: Trans. Path. Soc., vol. xlii, p. 77.
[‖] Wilson, J. A.: Medico-Chirurg. Trans., vol. xxiv, p. 221.
[**] Gairdner, W. T.: Clinical Medicine, 1862, p. 504.
[††] Dutton Steele: University Medical Magazine (Penn.), Feb., 1901, p. 838.

presence of gall-stones, to concomitant catarrh of the ducts, to a floating right kidney, or to twisting of the common bile-duct.

Dutton Steele[*] has collected 15 cases of hepatoptosis in which there were attacks of jaundice without gall-stones.

In Crawfurd's[†] case of anteverted liver the bile-duct had apparently been twisted, so as to give rise to jaundice, at the junction of the common bile and cystic ducts. The descent or dropping of the liver tends to produce this twisting. By injection experiments in the dead body Dutton Steele has shown that the more the liver descends towards the pelvis, the more difficult it is to drive injection from the biliary papilla into the gall-bladder.

(12) *Conditions of the Uterus, Ovarian Tumors, etc.*—The pressure of a pregnant uterus on the ducts has been regarded as responsible for jaundice (Murchison[‡]). This is very doubtful; mild jaundice in pregnant women is usually due to gastroduodenal catarrh, but may be due to gall-stones, cholangitis, or toxæmic inflammation of the small intrahepatic ducts. As mentioned elsewhere, the occurrence of acute yellow atrophy is especially favoured by pregnancy.

Ovarian tumors may exceptionally give rise to jaundice by pressing on the bile-duct. Poynder[§] has recorded such a case. On the other hand, jaundice may be merely associated with the presence of ovarian cysts and depend on catarrhal inflammation of the papilla, infective cholangitis, or gall-stones. The abdominal distension caused by an ovarian cyst favours stagnation of bile, infection of the ducts, and cholelithiasis. Thus suppurative cholangitis or cholecystitis may complicate ovarian cysts.

(13) *Constipation* may be associated with jaundice. Slight jaundice may possibly be due to absorption of poisons from the intestine producing catarrh of the intra-hepatic bile-ducts, or in other cases be due to the spread of associated duodenal catarrh to the common duct. In this way the relief of jaundice after free purgation may be explained. It seems improbable that fæcal accumulation by direct pressure can give rise to jaundice. But in rare cases where the colon is firmly united to the under surface of the liver by adhesions, fæcal accumulation in the transverse colon may possibly lead to kinking or compression of the common bile-duct.

GENERAL REMARKS ON THE DIAGNOSIS OF JAUNDICE.

The large number of conditions which may give rise to jaundice makes it essential that a careful examination should be made for any other evidence of disease. Thus the existence of a tumor in the abdomen, breast, or rectum will suggest malignant disease, while the coexistence of syphilis, either in the secondary or tertiary stage, should be an indication for specific treatment. The following points have a bearing on the nature of jaundice in a given patient.

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[*] Dutton Steele: University of Pennsylvania Med. Bull., vol. xv, p. 424, Jan., 1903.

[†] Crawfurd, R. P.: Lancet, 1897, vol. ii, p. 1182.

[‡] Murchison: Lectures on Diseases of the Liver, 2d ed., 1877, p. 358.

[§] Poynder: The Indian Med. Gaz., June, 1899, p. 208.

Age.—Slight and transient jaundice coming on within a few days of birth is benign or physiological, but if well marked and accompanied by constitutional symptoms and fever, should suggest a grave form of jaundice due either to septic infection of the umbilical cord or to some hæmic infection. (*Vide* p. 561.) Persistent jaundice from birth is in favour of congenital obstruction in the larger bile-ducts (*vide* p. 639) which is usually rapidly fatal, but in rare instances jaundice may persist from birth into adult life (*vide* Hereditary Jaundice, p. 562). In childhood and early adult life catarrhal jaundice is common. Between the ages of thirty and forty-five years gall-stones, especially in women, are the most probable cause, while later in life malignant disease and cirrhosis must be taken into account.

Sex.—Women are more prone to gall-stones and to malignant disease; men to cirrhosis and perhaps to the infectious forms of jaundice, such as Weil's disease, which have been noticed to attack soldiers and butchers. Pregnant women seem more susceptible than others to acute yellow atrophy.

Family Tendency to Jaundice.—The occurrence of jaundice in several members of the same family may be due to some acute infection, such as in Weil's disease, and is seen in epidemic jaundice. Chronic jaundice in members of the same family is met with in hypertrophic biliary cirrhosis and in some other allied and rare conditions (*vide* p. 309). The disease usually spoken of as congenital obliteration of the bile-ducts also has a tendency to attack infants of the same parents.

Onset.—If preceded by gastro-intestinal disturbance, catarrhal jaundice should be thought of; if by severe colic, gall-stones. A gradual onset with no special or striking symptoms should suggest the pressure of a tumor on the ducts. Repeated and transient attacks are in favour of gall-stones.

Occurrence of Pain.—Constant pain is suggestive of malignant disease; intermittent attacks point to gall-stones. Attacks of biliary colic may also occur when hydatid membranes are passed through the ducts and occasionally when malignant disease involves the ducts—pseudo-gall-stone colic. Absence of pain is, however, no proof against malignant disease, though it is the rule in catarrhal jaundice and common in cirrhosis.

Duration and Progress.—Jaundice of short duration is most commonly catarrhal or due to the passage of gall-stones. If continued for more than six months, it is highly unlikely that malignant disease is present, and biliary cirrhosis or impacted gall-stone should be thought of. Jaundice lasting for years is probably due to biliary cirrhosis.

Progressive and black jaundice suggest malignant disease, while chronic jaundice which varies from time to time is more compatible with a stone impacted in the common duct or biliary cirrhosis.

Degree and Intensity of Jaundice.—Slight icterus may be catarrhal, or, if associated with fever and constitutional disturbance, toxæmic.

The commonest causes of deep jaundice are malignant disease, impaction of a gall-stone in the common duct, and biliary cirrhosis. Extremely deep jaundice almost postulates malignant disease; that accompanying gall-stone impaction is deeper than that of cirrhosis, but never equals that seen in compression of the common bile-duct by tumors, such as carcinoma of the head of the pancreas, or in malignant disease of the duct.

Outbreaks of jaundice in epidemics suggest some form of toxæmic or infectious jaundice, such as Weil's disease.

Fever suggests toxæmic jaundice or, when associated with considerable splenic enlargement, biliary cirrhosis; pyrexia, of course, occurs in calculous cholangitis, in hepatic suppuration, such as abscess or pylephlebitis, and occasionally in malignant disease.

The condition of the gall-bladder is of great importance in the diagnosis of the cause of jaundice. It is not enlarged or palpable in cases of toxæmic or intra-hepatic jaundice, in biliary cirrhosis, or in cases where there is pressure on the hepatic ducts. Obstruction of the cystic duct usually leads to distension of the gall-bladder with mucous fluid. In obstruction of the common bile-duct by tumors pressing on it from without, such as carcinoma of the head of the pancreas, or arising in its walls, the gall-bladder is distended; on the other hand, in obstruction by gall-stones the gall-bladder, contrary to what might naturally be expected, is not enlarged. This is known as Courvoisier's law.

In 100 cases of obstruction of the common duct by causes other than calculi the gall-bladder was enlarged in 92, while of 87 cases of calculous obstruction the gall-bladder was shrivelled up and small in 70, or 80 per cent. (Courvoisier[*]). Mayo Robson,[†] Tuffier,[‡] Tessier,[§] and, quite recently, R. C. Cabot[‖] have supported Courvoisier's dictum. Cabot's figures are more striking than Courvoisier's, and show that the law is true in 95 per cent. of the cases.

The explanation of the shrivelled condition of the gall-bladder in gall-stone obstruction of the common duct is past cholecystitis.

Condition of the Liver.—Great enlargement occurs in malignant disease, hypertrophic biliary cirrhosis, and in abscess. But in abscess jaundice is slight or absent. In malignant disease the surface is generally nodular and the enlargement is progressive; in hypertrophic biliary cirrhosis the liver is smooth and the spleen is much enlarged.

The association of ascites points to malignant disease or cirrhosis, but in cirrhosis jaundice is usually less marked than in malignant disease.

The existence of disease elsewhere in the body has already been insisted on as of supreme importance in arriving at a diagnosis of the cause and, therefore of the prognosis and treatment, of jaundice.

[*] Courvoisier: Path. u. Chirurg. d. Gallenwegen, 1890.

[†] Mayo Robson: Gall-stones and Their Treatment. 1892

[‡] Tuffier: La Semaine Médicale, 1893, p. 55.

[§] Tessier: La Semaine Médicale, 1893, p. 7.

[‖] Cabot, R. C.: St. Paul Med. Journ., Dec., 1901.

PROGNOSIS.

The occurrence of jaundice in certain diseases is of importance as showing that hepatic complications have supervened; thus when, as very rarely happens, jaundice is met with in the course of typhoid fever, inflammation of the gall-bladder or ducts should be thought of. In puerperal eclampsia jaundice is of extremely bad omen; death usually follows in a few hours or days. The onset of jaundice after phosphorus poisoning is a sign that the liver is affected and must be regarded as of the most grave significance, since very few cases recover when this stage is reached. The onset of jaundice in a patient who has had malaria causes some anxiety at first, as it may be due to the severe hæmic infection of hemoglobinuric or "backwater" fever. Jaundice in relapsing fever makes the prognosis grave. (Sandwith.*)

The ultimate prognosis in any given case of jaundice depends not so much on the degree of jaundice as on the underlying cause. Thus the comparatively slight icteric tint (toxæmic jaundice) in some cases of pyæmia and the "black" jaundice of complete obstruction of the ducts in malignant disease do not differ very materially in their ultimate prognosis.

Prognosis in Chronic Jaundice.—When gall-stones in the common duct set up chronic jaundice there is a chance, though rather a slender one, that the calculus or calculi may pass and that a spontaneous cure may result. More commonly jaundice may disappear for a time as a result of bile escaping by the side of the gall-stone. Subsequently jaundice may return and may be accompanied by periodic attacks of pain, fever, and increase in jaundice or intermittent hepatic fever. In such cases the prognosis is good if operation for removal of the calculus is undertaken before the patient becomes weak or deeply jaundiced. But when continued fever has developed and there is reason to fear that suppurative cholangitis has supervened, the prognosis is very grave.

In chronic jaundice of hypertrophic biliary cirrhosis, though the chances of ultimate recovery are practically nil, life is often prolonged for years. In such cases the general state of nutrition and the length of the intervals between the exacerbations are points of importance in estimating the probable expectancy of life. Emaciation, weakness, and attacks repeated at short intervals point to death in the near future. In the rare but interesting conditions where jaundice is associated with splenic enlargement (splenomegalic jaundice, *vide* p. 308; and meta-icteric splenomegaly, *vide* p. 672) the prognosis is good, as the condition may go on for very many years. In the extremely rare condition of chronic hereditary jaundice (*vide* p. 562) the prognosis is good after the first few years of life, but should always be very guarded in an infant.

In very pronounced chronic jaundice, due to whatever cause, the prognosis is unfavourable, since if operation is undertaken, there is considerable danger from hæmorrhage, even though heroic doses of chloride of calcium are given before the operation. While if the patient is not operated upon, cholæmia will develop sooner or later. In such cases good effects from iodide of potassium point to gummatous obstruction and make the prognosis good.

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* Practitioner, vol. lxxii, p. 660.

In chronic jaundice due to malignant disease the prognosis is necessarily fatal, but it is not quite so desperate in cases presumed to be malignant disease of the pancreas as in cases where new-growth is palpable elsewhere. The explanation of this statement is that some cases formerly regarded as slow-growing ("scirrhus") carcinoma of the head of the pancreas are in reality chronic interstitial pancreatitis. (Mayo Robson.*)

In chronic jaundice much depends on the functional activity of the kidneys being well maintained; if the amount of urine falls and waste-products are less freely excreted, biliary toxæmia is likely to result. The presence of albuminuria points to the kidneys being damaged by the toxæmia accompanying the jaundice, and is, therefore, an index of a severe condition. The detection of leucin and tyrosin in the urine of a case of jaundice makes the prognosis very grave.

When jaundice is accompanied by hepatic insufficiency, so that poisons which should have been destroyed by the liver escape into the general circulation and give rise to a general toxæmia, as shown by nervous symptoms, such as delirium, drowsiness, and coma, and by hæmorrhages, the prognosis is very grave indeed, since life cannot be long maintained after the development of cholæmia. The occurrence, therefore, of nervous symptoms in cases of jaundice should always arouse anxiety.

There are cases at first quite indistinguishable from simple catarrhal jaundice in which nervous symptoms somewhat rapidly develop, and the cases then run the course of acute yellow atrophy of the liver. Again, in other instances the jaundice associated with malignant disease of the liver may begin exactly like catarrhal jaundice. Caution is, therefore, necessary in forming a prognosis in the early stages of what appears to be simple catarrhal jaundice, especially in patients past middle life.

When chronic jaundice is accompanied by xanthelasma or by the bulbous or "hippocratic fingers," it may be assumed that the cause of the jaundice is not malignant disease, inasmuch as this would have killed the patient before these changes would have had sufficient time to develop.

TREATMENT.

The radical and, of course, the only satisfactory course is the removal or cure of the underlying condition of which jaundice is a result; for this an accurate diagnosis in each case is essential. The methods of treatment in the various conditions giving rise to jaundice are dealt with elsewhere, and will not be repeated here. The necessity for a diagnosis of the cause in order to make successful treatment possible is shown by the cure of jaundice in the early stage of syphilis by mercury, or when due to the pressure of a gumma on the ducts by iodides, or surgically by the removal of calculi from the common bile-duct in intermittent hepatic fever.

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* Mayo Robson: Lancet, 1900, vol. ii.

In a large number of cases jaundice depends on catarrhal inflammation of the ducts, and the removal of this condition can often be effected by medical measures which increase the flow of bile and so flush the bile-ducts, *e. g.*, draughts of water containing salts in solution, drinking the water at a spa, such as Carlsbad, Vichy, etc., and the administration of salicylates. In some cases medical measures fail to remove catarrhal inflammation of the ducts and surgical interference in the form of free drainage may be necessary.

Symptomatic or Palliative Treatment of Jaundice.—Constipation should be prevented by exercises, plenty of water, salines, such as phosphate and sulphate of soda, sulphate of magnesia, or the natural Carlsbad or other purgative waters, taken on an empty stomach before breakfast. If necessary, a few grains of calomel or of blue pill may be taken the night before. Vigourous purgatives should be avoided, as intestinal catarrh may be thus set up, or, if present, increased. For gastric catarrh careful dieting, bicarbonate of soda, and for vomiting bismuth, dilute hydrocyanic acid, and warm applications to the abdomen should be ordered. For flatulence minute doses ($\frac{1}{40}$ grain) of calomel or of liquor hydrargyri perchloridi, salicylate of bismuth, creasote, turpentine in capsules, or salol may be given.

Fresh ox bile contained in capsules or keratin-coated pills, so as to pass unaltered through the stomach, are sometimes given to replace the absent bile in the bowel, and may be taken three times a day before food.

For pruritus, which is often extremely troublesome, and, if unrelieved, may lead to great disturbance of the night's rest and sleeplessness, the skin may be sponged with carbolic acid lotion 1 : 40, or the patient may take an alkaline or an acid bath. An acid bath containing nitrohydrochloric acid is given in a wooden bath, the patient remaining in it for about twenty minutes.* Hypodermic injection of pilocarpine, $\frac{1}{8}$ to $\frac{1}{4}$ grain, is often employed with relief. Thyroid extract has been found to give relief by Gilbert and Herscher.† Antipyrin is recommended by R. Crocker‡ on account of its sedative action on the nervous system. For itching of the skin and hæmorrhages the administration of chloride of calcium in 15 or 20-grain doses may be tried three times a day for two or three days, but not longer at a stretch, as its effect in promoting coagulation of the blood is lost after a comparatively short time.

Before an operation, such as a cholecystotomy, on a jaundiced patient it is well to give chloride of calcium so as to diminish the risk of bleeding from the jaundiced tissues.

Milk is the most satisfactory food in the early stages, and as long as jaundice is progressive, since it is easily digested, minimises intestinal putrefaction and fermentation and acts as a diuretic. The patient's inclination should be consulted, and when appetite returns, boiled rice, chicken, fish, and a little meat may be given. Fatty food, for which jaundiced patients often have a marked distaste, should be avoided. Alcoholic drinks are also contraindicated.

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* Tanner's Index of Diseases, 4th ed.

† Gilbert and Herscher: Le Bulletin Médical, July 30, 1902.

‡ Crocker: Diseases of the Skin, 2d ed.

Even in cases of inoperable malignant disease, such as carcinoma of the head of the pancreas, surgical measures may still give some relief by removing the extreme jaundice. Cholecystenterostomy, or uniting the gall-bladder to the small intestine, allows the bile to enter the intestine and thus removes the jaundice, prevents the occurrence of biliary toxæmia or cholæmia, and greatly improves the patient's condition for a time. The operation must be performed early; if "black jaundice" has already developed, the patient is in a very unfavourable state for this procedure.

JAUNDICE IN THE NEWLY BORN.

Jaundice occurring within a few days or weeks of birth has such special bearings that it requires separate consideration. The term icterus neonatorum has been specially employed for the simple jaundice so commonly seen within a few days of birth, but it is better to use it as a general description for jaundice at or shortly after birth.

A number of different forms of jaundice may attack newly born infants.

As many as nine varieties have been tabulated by Skormin: (i) Benign jaundice; (ii) septic, due to umbilical infection; (iii) infective jaundice; (iv) Winckel's disease; (v) catarrhal jaundice; (vi) toxic jaundice, due to drugs, such as carbolic acid, resorcin; (vii) jaundice following hæmorrhages into the skin; (viii) jaundice of acute yellow atrophy; (ix) various forms of obstructive jaundice.

Some of the forms are extremely rare; thus Skormin* could only refer to seven examples of acute yellow atrophy in infants. From a practical point of view jaundice in infants may be conveniently divided into two main groups: (i) Those which are mild and tend to recover; (ii) the severe forms in which the prognosis is grave.

MILD FORMS OF JAUNDICE IN THE NEWLY BORN.

The mild or innocent forms of jaundice in the newly born are: (*a*) Idiopathic, simple, or physiological jaundice. (*b*) The mild infective or catarrhal.

IDIOPATHIC, SIMPLE, OR PHYSIOLOGICAL JAUNDICE.

Etiology.—It is, like many diseases, commoner among the poor, and is known under the name of the "yellow gum." It is thought to be more frequent in premature and feeble infants with deficient resistance, and has been said to be commoner in males than in females (J. L. Steven), but it is doubtful whether this is so. It has been suggested that if the cord is ligatured late, so that the infant obtains a maximum of the placental blood, icterus, presumably depending on increased hæmolysis, is more likely to result.

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* Skormin: Jahrb. f. Kinderheilk., Aug., 1902. Epitome, Brit. Med. Journ., 1902, vol. ii, No. 308.

Bauzon,* however, from a consideration of 240 cases, came to the conclusion that, far from favouring the occurrence of jaundice, delayed ligation of the umbilical cord improved the resistance of the infant and thus tended to prevent the onset of icterus.

There is no proof that delayed birth or abnormal presentations, such as a breech, are important factors.

The occurrence of jaundice so soon after birth has naturally been thought to depend on events special to birth and the first few days of independent existence. Birch-Hirschfeld thought it might depend on vascular engorgement of the liver leading to œdema of the portal spaces, and thus to pressure on the bile-ducts. The postmortem observations of Cohnheim failed to lend any support to this view. Moreover, œdema of the portal spaces, though it may be associated with jaundice, for example, when there is a tumor pressing on the bile-ducts and lymphatic vessels, does not of itself induce jaundice.

Quincke† suggested that, owing to patency of the ductus venosus, bile absorbed from the intestine and on its way to the liver passed from the portal vein directly into the inferior vena cava and so into the general circulation.

It is tempting to associate the microbic invasion of the previously sterile intestine with the appearance of jaundice, especially as the bile is often very viscid. There is another factor which, when taken in conjunction with microbic infection of the alimentary canal, may help to account for icterus neonatorum. In the newly born there is an increased number of red blood-corpuscles (hyperglobinæmia) and a correspondingly increased hæmolysis. This would normally lead to an increased production of bile, and if, from microbic activity, there was even slight inflammation of the ducts, diffusion of bile into the lymphatics and jaundice would readily result.

Morbid Anatomy.—When such a jaundiced child dies from accident or from other disease, there is widespread staining of the organs and tissues of the body with the exception of the liver, kidneys, and spleen. It is remarkable that the brain, spinal cord, and cartilages which are not stained by bile-pigment in the jaundice of adults are distinctly coloured by the bile in this unimportant condition. The liver cells contain a good deal of bile-pigment, but there are no other changes; the ducts are normal, and bile can be squeezed from the gall-bladder into the duodenum. The bile is sometimes found to be peculiarly viscid. (Still.‡) The pericardial fluid contains bile acids and bile-pigment, showing that there is true jaundice. The kidneys, as is so commonly the case in the newly born, show masses ("infarcts") of uric acid in the collecting tubules.

Incidence.—It occurs in from 30 to 80 per cent. of infants. It is said to be more frequent in lying-in hospitals than in private life. But Holt's * figures from the Sloane Maternity Hospital of 900 births with 300 cases of jaundice (intense in 88, mild in 212) give about the lowest incidence. Steven,† by adding up various statistics, found that it occurred 1212 times in 2086 children, or in 58.1 per cent. In 248 newly born infants examined by Porak‡ it occurred in 80 per cent.

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* Bauzon: Le progrès Médical, April 14, 1899.
† Quincke: Archiv f. exper. Path. u. Pharmak., 1885, Bd. xix.
‡ Still, G. F.: Clinical Journal, vol. xvii, p. 323, March 13, 1901.

Clinical Characters.—It comes on within the first four days of life, most commonly on the second or third day, and lasts from one to two weeks. In some instances it persists longer, and after arousing a suspicion that there is some more serious factor at work, eventually passes away. After its appearance it increases both in extent and in intensity for about a couple of days and then gradually diminishes. There are no symptoms whatever connected with the presence of the jaundice—the temperature, pulse, appetite, and fæces are normal. The urine is free from bile except in exceptionally marked cases, and there is no albuminuria. The jaundice begins on the face, chest, back, and extends to the abdomen, limbs, and lastly to the hands and feet. The jaundice shows up more prominently because of the general cutaneous engorgement of the newly born infant. The staining is perhaps best seen on the back, and can be distinguished from the normal redness of the infant by pressing the blood out of the cutaneous vessels when the skin remains jaundiced. The gums may be seen to be yellow. The sclerotics are not always yellow. A division has been made into the slightest cases, where the whites of the eyes are unaffected, and those where the conjunctivæ show an icteric tint.

Porak described three classes—(*a*) The staining is slight and passes away in four days, and involves the face, back, and chest, but the conjunctivæ are not affected. (*b*) The jaundice extends to the abdomen, arms, and thighs, while the conjunctivæ may or may not be affected. (*c*) There is universal jaundice and the conjunctivæ are always involved.

It is difficult to give a satisfactory explanation of the curious facts that the sclerotics are affected later and in a less degree than the skin; exactly the reverse of what occurs in ordinary jaundice. It is possible that it may depend upon the hyperæmic state of the skin and the correspondingly large amount of blood, containing bile, that passes through the vessels of the surface of the body.

Diagnosis.—It is distinguished from the normal reddish-brown tint of the young infant by pressing on the skin and finding that the yellow discolouration remains after the vessels have been obliterated. Its short duration prevents any confusion with congenital obliteration of the ducts; in the rare instances of more prolonged simple jaundice there is an absence of the enlarged and firm liver and spleen seen in the former condition. It must be distinguished from the grave forms of jaundice, such as septic infection of the umbilical vein, syphilitic disease of the liver, and Winckel's disease, by the healthy condition of the patient, the absence of fever, and, indeed, of every sign or symptom except jaundice.

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* Holt, E.: Quoted by Osler, Practice of Medicine, p. 551, 4th ed.

† Steven, J. L.: Glasgow Medical Jour., 1897, vol. xlvii, p. 4.

‡ Porak: Rev. Mens. de Med., 1878, p. 342.

Prognosis.—In this condition, for it cannot be called a disease, the outlook is perfectly cloudless. But in cases of jaundice in the newly born there is always the question whether the jaundice is "physiological" or whether it is the first sign of some grave organic or septic change. The prognosis of jaundice in the first few days is, therefore, very difficult in the absence of any definite diagnosis. No special form of treatment is required.

CATARRHAL OR MILD INFECTIOUS JAUNDICE.

In the first few days of life the alimentary canal normally becomes invaded by micro-organisms, and sometimes the infection is more or less virulent. The grave forms of infectious jaundice are described on page 561. The mild forms of infectious jaundice are much the same as the catarrhal jaundice of adults, and clinically I do not think that any reliable distinction can be drawn between mild infections and catarrhal jaundice. Many writers, however, consider that catarrhal jaundice is almost unknown in infants. Skormin* refers to but three recorded cases.

The disease may occur in epidemics or sporadically.

Lesage and Demelin † have described a small epidemic and have specially studied the characters of the disease.

It may occur in the first few days of life and in breast-fed infants. There is loss of appetite; vomiting may occur, but though so common in infants, it is not specially noticeable in this form of jaundice; there is also diarrhœa, jaundice, slight fever, and drowsiness. Lesage and Demelin lay stress on the appearance of cyanosis and on the fact that the stools, which may contain bile, are alkaline or neutral instead of being acid. The jaundice is universal and the urine contains bile-pigment, but the stools need not be devoid of bile. The prognosis is good.

Treatment.—The infants should be kept warm, but the room should be well ventilated. Water should be freely given, and fractional doses of calomel or gray powder should be given five or six times daily.

SEVERE FORMS OF JAUNDICE IN THE NEW-BORN.

The severe forms of jaundice which affect the newly born may be divided into—

(1) Those due to very definite obstruction or organic change, such as obliteration of the ducts (*vide* p. 639), syphilitic disease of the liver (*vide* p. 373), or, in very rare instances, gall-stones.

(2) Virulent infections, either of a local nature, as in umbilical vein infection, or in general hæmic infections, as in Winckel's disease.

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* Skormin: Jahrb. f. Kinderheilk., Aug., 1902.

† Lesage and Demelin: Rev. de Méd., 1898, Jan., p. 14.

JAUNDICE DUE TO DEFINITE OBSTRUCTION OR ORGANIC CHANGE.

Congenital obliteration of the ducts (p. 639) and jaundice occurring in hereditary syphilitic disease of the liver (*vide* p. 373) are dealt with elsewhere.

Gall-stones.—In very rare instances gall-stones are found in the newly born. Still* has collected ten cases either in still-born infants or infants dying within a few weeks of birth. Seven of these were jaundiced. It, therefore, appears that gall-stones must be regarded as a rare cause of severe jaundice in the newly born. Thomson† puts forward the suggestion that the inflammation of the biliary tract which induces cholelithiasis in infants is probably of the same nature as that responsible for congenital obliteration of the ducts. (*Vide* p. 639.)

SEVERE INFECTIVE FORMS OF JAUNDICE.

Umbilical Infection.—A very fatal form of jaundice is associated with infection of the navel in the newly born. There is suppurative phlebitis of the umbilical vein. This form of pyæmia formerly gave rise to a very high mortality among infants born in lying-in hospitals, and has been prevented by cleanliness and antisepsis. According to Cantlie,‡ it is very common in Hong-Kong. Hæmorrhage may occur from the umbilical wound.

The infection may be conveyed from the mother and is streptococcal. At the postmortem examination there is suppurative phlebitis of the umbilical vein, and the liver is pale and shows areas of small-cell infiltration in the portal spaces. There may be other pyæmic manifestations, such as peritonitis, pleurisy, meningitis.

There is jaundice, accompanied by fever and evidence of local suppuration at the umbilicus, which is red and swollen.

There are vomiting and diarrhœa; the respiration and pulse are rapid. The child is first restless, and then becomes comatose. Death may be due to hæmorrhage from the umbilicus or from the gastro-intestinal tract.

Grave Forms of Jaundice due to General Infections.—Septicæmia may give rise to toxæmic jaundice in the newly born at the same time that the severity of the general hæmic infection produces hæmorrhages and hæmaturia. It may be sporadic, as in pyæmia secondary to suppurative arthritis or to infected epiphyseal disease in congenital syphilis.

Epidemic Forms of Grave Infective Jaundice.—Epidemics of jaundice in infants accompanied by diarrhœa, hæmaturia, and attended with great mortality were described by Pollak,§ Laroyenne,‖ Parrot,** and Winckel.†† Winckel described an epidemic, which proved fatal to 23 out of the 24 infants attacked, under the name of pernicious icteric cyanosis.

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* Still, G. F.: Trans. Path. Soc., vol. l, p. 151.

† Thomson, J.: Edinburgh Hospital Reports, vol. v, p. 1.

‡ Cantlie: Encyclopædia Medica, vol. vii, p. 41.

§ Pollak: Wiener med. Presse, 1871.

‖ Laroyenne: Congrès pour l'avancement des Sciences, Lyon, 1873.

** Parrot: Archiv Physiolog. norm. et path., 1873, p. 512.

†† Winckel: Deutsche med. Wochen., Bd. v, S. 303, 1879.

This disease in the newly born has been called Winckel's disease. It is regarded by Lesage and Demelin as a very severe form of infection of intestinal origin, corresponding to the mild form of infectious or catarrhal jaundice. It is probably a severe form of septicæmia, and closely resembles Buhl's disease, in which there are jaundice, gastro-intestinal hæmorrhages, with infarcts and acute fatty degeneration of the organs of newly born infants.

The clinical features are mainly those of a severe septicæmia occurring in epidemics among newly born infants and accompanied by hæmaturia and jaundice. The skin has a bronzed appearance, probably due to a combination of jaundice and the cyanotic condition of the skin. An important feature is hæmaturia; Winckel, however, described hæmoglobinuria. The condition is extremely fatal, and treatment is practically useless. Treatment should be directed to removing the contents of the bowels by purgatives and enemata. Minute doses of calomel should be given every two or three hours until eight or ten doses have been given, so as to disinfect, as far as possible, the intestinal tract. The disease differs from umbilical phlebitis in the absence of any signs of local inflammation about the navel, and in the slighter degree of fever.

HEREDITARY JAUNDICE.

Jaundice may occur in parents and children and be an acquired condition, probably due to some factor which attacks both generations at the same time. Examples of hypertrophic biliary cirrhosis in parents and children have been recorded by Boinet,[*] and by Boix[†] (*vide* p. 309), but are more probably dependent on environment than on heredity. Cases in which periodic attacks of jaundice associated with splenic enlargement have appeared to be hereditary have been described by C. Wilson,[‡] who gave an account of a family in which members in three successive generations were affected, and by Barlow and Shaw.[§] These cases, which are rather obscure in their etiology, appear to form a kind of connecting link between biliary cirrhosis and chronic splenic anæmia.

A few isolated observations, such as those of Cocking,[‖] Arkwright,[**] and A. Pick,[††] have been made, which raise the question whether hereditary jaundice may depend on slight congenital abnormalities in the bile-ducts; Pick, however, opposes this view, and suggests a congenital communication between the bile-ducts and the lymphatics. Parkes Weber[‡‡] puts forward the view that there is obliterative cholangitis of one or more of the smaller intra-hepatic ducts.

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[*] Boinet: Archiv. général. de Méd., t. clxxxi, p. 385, April, 1898.
[†] Boix: La Presse Médicale, March 16, 1898.
[‡] Wilson, C.: Trans. Clinical Soc., vol. xxiii, p. 162.
[§] T. Barlow and Batty Shaw: Trans. Clinic. Soc., vol. xxxv, p. 155.
[‖] Cocking: Quarterly Med. Journ. (Sheffield), vol. xi, p. 104, 1903.
[**] Arkwright: Edinburgh Med. Journ., Aug., 1902.
[††] Pick, A.: Wien. klin. Wochens., 1903, S. 493.
[‡‡] F. Parkes Weber: Edinburgh Med. Journ., vol. xiv, p. 111, Aug., 1903.

In Arkwright's report a woman who, when four years old, had jaundice herself, had 15 children, 14 of whom had jaundice, 4 surviving. Cocking described a woman aged fifty years who had been jaundiced since she was three weeks old and had lost one child with jaundice at the age of fifteen weeks. Pick recorded a family in which the mother and three children, between the ages of thirty-five and twenty-six years, had been jaundiced since birth; in these cases the urine did not contain bile-pigment and the fæces did, so the condition may have been different from that in Arkwright's and Cocking's cases, and more allied to family cholæmia.

In some of these hereditary cases jaundice persists throughout life and is compatible with fair health.

The condition of subicterus, described as simple family cholæmia and as a diathesis rather than as a fully developed disease, should be mentioned in connexion with hereditary jaundice.* The subjects of this diathesis are specially prone to jaundice, biliary cirrhosis, cholelithiasis, and may be compared to persons specially liable to bronchitis, pharyngitis, or diarrhœa.

ICTERUS GRAVIS.

Icterus gravis, or malignant jaundice, is a term which is somewhat loosely used for cases of toxæmic jaundice of a severe type which tend to end fatally and show extensive degeneration of the liver cells. It thus includes a number of different conditions, such as the most severe cases of febrile jaundice or Weil's disease, acute yellow atrophy of the liver, phosphorus and other forms of mineral poisoning, and other cases where an acute toxæmic or infective condition of the body falls on the liver and gives rise to widespread acute degenerative and necrotic changes in the liver cells; for example, in yellow fever and in streptococcal and staphylococcal hæmic infections. The term icterus gravis may also appropriately be applied to cases where acute degenerative changes are superimposed on some pre-existing disease of the liver, such as cirrhosis or nutmeg liver.

Icterus gravis should, therefore, be regarded not as a specific disease, but as a group of symptoms, due to the rapid development of hepatic insufficiency, eventually becoming absolute, which may be due to many different causes.

Icterus gravis may be divided into—(*a*) Those cases where the liver was previously healthy—*e. g.*, in phosphorus poisoning, acute yellow atrophy, and yellow fever. (*b*) Those cases where it supervenes as a terminal lesion on pre-existing hepatic disease—*e. g.*, in cirrhosis or chronic venous engorgement.

The following classification, though based on different grounds, is given by Boix† and is much the same:

Specific and primary icterus gravis:	In phosphorus poisoning. In yellow fever. Essential (acute yellow atrophy).
Non-specific and always secondary:	In staphylococcal and streptococcal infections. In infection with the colon bacillus.

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* Gilbert and Lereboullet: Gaz. Hebdom. de Méd. et de Chirurg., 1902, p. 889.

† Boix: Manuel de Médecine, edited by Debove and Achard vol. vi, p. 342.

Acute yellow atrophy is a special form of icterus gravis and may be regarded as a typical variety, since it is uncomplicated by the presence of any other disease. The terms icterus gravis and acute yellow atrophy are not absolutely synonymous, for all cases of icterus gravis do not show the naked-eye appearance of acute yellow atrophy, though the change—acute degeneration in the liver cells—is essentially the same in both. Under the microscope the appearances are so closely allied that from a pathological point of view they may be said to pass into each other. Cases of acute yellow atrophy are often described as icterus gravis, and, conversely, cases of icterus gravis are sometimes reported under the heading of acute yellow atrophy.

Since some of the various conditions, such as acute yellow atrophy, phosphorus poisoning, and Weil's disease, which are or may be included under the generic term icterus gravis, will be separately described, the clinical features of icterus gravis will not require any further description than that found under the heading of acute yellow atrophy. Generally speaking, the liver is somewhat enlarged in icterus gravis and the degenerative changes are not so uniform or so markedly necrotic as in acute yellow atrophy. The morbid changes described under the heading of Acute Hepatitis may be present in cases of icterus gravis, or in some instances very extensive fatty change. (*Vide* p. 425.) In icterus gravis due to staphylococcal and streptococcal infection the temperature is raised, while in other instances, where the infective agent has been thought to be the colon bacillus, the temperature is, as in phosphorus poisoning, depressed. (Hanot,[*] Boix.[†])

ACUTE YELLOW ATROPHY.

Synonym: Acute Atrophy of the Liver.

Definition.—An acute degeneration of the liver cells with diminution in size of the liver, accompanied by jaundice, fever, nervous symptoms, and usually a fatal termination.

The history of acute yellow atrophy has been most carefully investigated by Dr. J. Wickham Legg[‡] in his elaborate account of the disease, to which every subsequent writer on the subject must refer. The earliest case that he has unearthed is one by Ballonius, who died in 1616. Bright,[§] in 1836, described the condition as due to acute inflammation, and gave a good coloured drawing of the liver.

INCIDENCE AND ETIOLOGY.

That the disease is rare is shown by the fact that no case occurred in the first eleven years' work of the Johns Hopkins Hospital, Baltimore, and that Osler,[‖] in the third edition of his Practice of Medicine, says that he had never seen a case. Curiously enough, some observers have met with a succession of cases in quite a short time. Reiss saw five cases in three months and Arnold four in a similar period.

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[*] Hanot: Archives général. de Méd., t. clxxvii, p. 77, 1896.
[†] Boix: Archives général. de Méd., t. clxxviii, p. 217, July, 1896.
[‡] Wickham Legg: Bile-Jaundice and Bilious Diseases, p. 416.
[§] Bright, R.: Guy's Hospital Reports, vol. i, p. 613, 1836.
[‖] Osler: Practice of Medicine, 3d and 4th ed.

In twenty years I have seen in the postmortem room or examined the livers of seven cases.

Up to 1894 W. Hunter* was only able to refer to 250 published cases, and in the succeeding four years McPhedran † collected 29 more. In twenty-five years 7 cases occurred at St. Bartholomew's Hospital, which, according to Brunton and Tunnicliffe,‡ is 1 in every 500,000 applications for treatment at that charity. In twenty-seven years there were 11 cases brought to autopsy at Guy's (Hilton Fagge §).

Age.—It is commonest between the ages of twenty and thirty. According to Hunter's figures, half the cases occur in this decade, and four-fifths between the ages of ten and forty. A certain proportion—I have collected 22 such cases—occur within the first ten years of life; while in rare instances it has been seen within the first year or even shortly after birth.

Skormin ‖ refers to 7 published instances of acute yellow atrophy in newly born infants.

In connexion with the occurrence of cases in very early life the resemblance between some cases of icterus gravis and rather rapid pericellular cirrhosis of hereditary syphilis must be borne in mind.

The youngest case in which I have had the opportunity of cutting sections of the liver was in a child aged two years; the liver weighed 11 ounces, and showed the naked-eye and microscopic appearances of acute yellow atrophy. I am indebted to Dr. Schorstein and Dr. O. Grünbaum for the liver of this case.

Sex.—Females are more often attacked than males, the proportion between the two being nearly 2 to 1. This greater incidence of the disease in women seems to depend on a special association between pregnancy and this disease. The influence of *pregnancy* is borne out by the fact that a large proportion of the cases occur in connexion with this event. The liver appears to be peculiarly susceptible to morbid changes during pregnancy, and there is reason to believe that degenerative changes in the liver play a very important part in the production of puerperal eclampsia. It is not improbable that the discrete focal necrosis in the liver seen in eclampsia represents in a lesser degree or in an earlier stage the changes of acute yellow atrophy. Statistics show that acute yellow atrophy occurs most often between the fourth and seventh months of pregnancy.

Mental disturbance, shock, or fright has preceded the onset of the disease in a certain number of cases. The mental worry in persons with syphilis or in women that are pregnant, especially if unmarried, may tend further to depress the resistance of the body and to dispose to the disease.

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* Hunter, W.: Allbutt's System of Medicine, vol. iv.

† McPhedran, A.: Sajous' Annual, 1899, vol. iv, p. 393.

‡ Brunton and Tunnicliffe: St. Bartholomew's Hosp. Reports, vol. xxxii.

§ A Text-book of Medicine, edited by Pye Smith, vol. ii, p. 544, 4th ed., 1902.

‖ Skormin: Jahr. f. Kinderheilk., Aug., 1902.

In six fatal cases, recorded by Hardie,* of acute yellow atrophy of the liver in Australia, importance was attached to the anxiety and fear with which women look forward to parturition in hot climates.

Syphilis.—The secondary stage of syphilis is sometimes accompanied by jaundice, which is usually harmless and yields to specific treatment. In rare instances acute yellow atrophy supervenes. This is said to be more often seen in women than in men. The syphilitic toxine would appear to attack the liver acutely, just as it sometimes attacks the spinal cord, giving rise to acute myelitis.

In 72 cases of acute yellow atrophy syphilis was noted as a causal factor in 7 (Lebert†). In 9 cases of acute atrophy following syphilis collected by Chauffard,‡ 7 were in women. I have references to 28 cases of post-syphilitic acute atrophy of the liver.

In some of the cases the jaundice has run a long course, and although the morbid appearances are like those of acute yellow atrophy, it is probable that for a considerable time the jaundice is due to pericellular cirrhosis and that a terminal and acute degeneration of the liver cells develops. This would place the cases in the category of icterus gravis.

In a case reported years ago Hilton Fagge § drew particular attention to the resemblance between the appearances of pericellular cirrhosis and those in a case of acute atrophy supervening on the secondary stage of syphilis.

As already mentioned, the mental anxiety experienced by persons who are aware that they have contracted syphilis has been thought to play a part in the production of acute atrophy.

Talamon ‖ has described an interesting case in which a severe fright in a girl aged seventeen, who had secondary roseola, enlarged glands, and condylomata at the time, was followed within eighteen hours by "emotional jaundice"; this lasted three weeks and symptoms of acute yellow atrophy, hæmorrhages, delirium, and convulsions carried her off on the twenty-ninth day. The liver was in a state of acute parenchymatous and interstitial inflammation. In this case the emotional jaundice seems to have rendered the liver more susceptible to the effects of the syphilitic toxine.

The following case, for which I am indebted to Dr. A. H. Wilson, illustrates some of the features of acute yellow atrophy due to syphilis. A girl aged seventeen, with a sore on the right labium and a roseolous rash, became jaundiced six weeks before death. Three days later she began to vomit and continued to do so until her death; at no time was there blood in the vomit. Three weeks before death jaundice increased, her mental condition was affected, delirium supervened, and the urine and fæces were passed involuntarily. She became extremely hungry and suffered from thirst. She was admitted to the South Devon and East Cornwall Hospital in a state of collapse twenty-four hours before her death. There were bile-pigment, leucin, and tyrosin in the urine. She died comatose. The liver, which I examined microscopically, showed great destruction of the liver cells and hæmorrhages, with some pre-existing fibrosis often passing between the cells. These appearances suggested a combination of pericellular cirrhosis and acute necrosis of the cells.

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* Hardie, D.: Australian Med. Gaz., May, 1890.

† Lebert: Virchow's Archiv, Bd. vii, S. 383.

‡ Chauffard: La presse Méd., Aug. 11, 1897.

§ Hilton Fagge: Trans. Path. Soc., vol. xviii, p. 136.

‖ Talamon: La Médecine Moderne, Feb. 13, 1897.

Alcoholic excess in a few instances has apparently stood in a causal relation to acute yellow atrophy, since the disease has been noted to come on after recent and undoubted excessive indulgence.

Thierfelder * refers to six such cases among his 143 cases of acute atrophy, and cases have been described by Moxon,† Cayley,‡ Carrington,§ Musser.‖

Acute yellow atrophy may occur in chronic drunkards, and acute atrophy has been described as supervening on existing cirrhosis. Thierfelder quotes eight cases of this kind. It must, however, be borne in mind that cases of protracted acute atrophy may show some recent fibrosis. Inasmuch as alcohol is a protoplasmic poison, it is not improbable that the resistance of the liver being diminished by alcoholic excess, other causes making for acute yellow atrophy are thus enabled to become effective.

Chloroform narcosis has in most exceptional instances been followed by acute yellow atrophy. Chloroform has a toxic effect on the liver cells, but is so rarely seen in practice that additional factors, such as sepsis and diminished resistance of the liver, must be necessary to explain the occurrence of acute yellow atrophy after the administration of chloroform. (Compare p. 425.)

Max Ballin ** has collected nine fatal cases of acute yellow atrophy after operations.

The Influence of Pre-existing Hepatic Disease.—The lesions of acute yellow atrophy may supervene in the course of diseases of the liver, such as cirrhosis, catarrhal jaundice, chronic venous engorgement, or gall-stone obstruction. The onset is, no doubt, disposed to by the morbid condition of the organ. In these cases it is more convenient to describe the condition as icterus gravis rather than as acute yellow atrophy. Impaired vitality and resistance on the part of the liver must render it more susceptible to acute infectious or toxic influences, and so to acute atrophy. This very probably accounts for the influence of pregnancy in disposing to acute yellow atrophy. The occurrence of such a rare disease in two sisters (Graves ††), and in a brother and sister (Griffin ‡‡), suggests the possibility that congenital want of resistance may be a factor of importance.

Relation to Phosphorus Poisoning.—Inasmuch as there is a marked resemblance between the clinical features of acute yellow atrophy and phosphorus poisoning, and since the nature of the change in the liver cells is essentially the same, viz., one of acute degeneration, it has been thought that all cases of acute yellow atrophy are due to phosphorus poisoning. In support of this it might be urged that examples of what were for a time considered undoubted instances of acute yellow atrophy have on further enquiry turned out to be due to phosphorus poisoning. Poore,* who quotes cases of this kind, unhesitatingly believes that clinically and pathologically the two conditions are indistinguishable.

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* Thierfelder: v. Ziemssen's Cyclopædia of the Practice of Medicine, vol. ix, p. 245.

† Moxon: Trans. Path. Soc., vol. xxiii, p. 138.

‡ Cayley: Trans. Path. Soc., vol. xxxiv, p. 127.

§ Carrington: Trans. Path. Soc., vol. xxxvi, p. 221.

‖ Musser: American Journ. Med. Sciences, vol. lxxxvii, July, 1884.

** Max Ballin: Annals of Surgery, March, 1903, p. 362.

†† Graves: Clinical Medicine, p. 459.

‡‡ Griffin: Dublin Journal of Medical and Chemical Science, 1834.

Generally speaking, however, the differences between the two conditions are sufficiently definite to separate them, and we are certainly not justified in assuming that all cases of acute yellow atrophy are due to phosphorus poisoning. These differences between the liver in phosphorus poisoning and acute yellow atrophy are—

(1) In acute yellow atrophy the diminution in size is practically constant, whereas in phosphorus poisoning enlargement is the rule. (2) In acute yellow atrophy the changes in the liver cells lead to rapid disintegration with but slight increase in the amount of fat; while in phosphorus poisoning there is very extensive fatty metamorphosis of the liver cells, the amount of fat in the organ reaching 30 per cent. as against 5 per cent. in acute yellow atrophy.

Schmaus,† however, believes that these differences are merely a matter of time and that as death occurs more rapidly in phosphorus poisoning, there is not time for the absorption and removal of fatty and degenerative products. When life is prolonged, the condition resembles that of acute yellow atrophy.

It may be safely stated that they are closely allied forms of icterus gravis, but at present, for purposes of clinical practice, it is convenient to regard them as distinct entities.

MORBID ANATOMY.

Weight and Size.—The liver is always greatly diminished in size; in fact, cases otherwise resembling acute atrophy, in which the organ is large, belong to the allied condition of icterus gravis, for diminution in size is an essential part of acute yellow atrophy. It may weigh half or a third of its normal weight. Twenty-eight ounces is not uncommonly found instead of the normal (53 ounces in males, 45 ounces in females). The atrophied condition is usually fairly universal, but the left lobe is often in a more advanced state than the remainder, and the change is often thought to begin there. In acute cases the surface is smooth and flaccid. In cases which have had a prolonged illness—several weeks or months—adenomatous nodules resembling new-growths may be seen on the surface.

They have been described in cases which died one and a half to two years after the onset of acute symptoms. In Steinhaus'‡ case the total duration was twenty-one months and in Stroebe's § two years.

They are due to compensatory hyperplasia of the liver cells, and are therefore analogous to the multiple adenomata in cirrhosis. These protracted cases merge into a condition of nodular parenchymatous hepatitis.*

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* Poore, G. V.: Nervous Affections of the Hand and Other Clinical Studies, p. 166, 1897.

† Schmaus: A Text-book of Pathology and Pathological Anatomy, p. 396 American translation, 1903.

‡ Steinhaus: Prag. med. Wochen., 1903, S. 323.

§ Stroebe: Ziegler's Beiträge, Bd. xxi, S. 379, 1897.

Cayley † described and figured a good example of acute atrophy in which there were definite tumor-like projections from the surface of both lobes of the liver. In the figure accompanying the account the projections seem to correspond with the yellow atrophy and the depressed areas with red atrophy. There is a somewhat similar specimen from a child in the museum of Charing Cross Hospital. In MacCallum's ‡ case these hyperplastic nodules were green in colour.

The capsule is wrinkled and loose, so that it can be picked up by the fingers, like the walls of a half-filled bladder. If a stream of water is turned on to the organ, the capsule is thrown into folds and wrinkles. It can be peeled off quite easily in many cases. Externally the organ has a greenish-yellow colour, often relieved by red splashes. There may be small hæmorrhages under the capsule. The liver is flabby and limp, and collapses and bends under its own weight; thus it readily doubles over on itself and is without the rigidity of a normal liver. This flabbiness of the organ during life allows it to drop back from the abdominal wall, its place being taken by the colon. As a result, the liver dulness may be entirely absent. The liver cuts with the same kind of resistance that collapsed lung does, and though very flabby, is not softer or more easily broken down by the finger than in health. Many writers, however, state that the liver is softened. Possibly this is more true in icterus gravis. If kept for some time, the surface of the liver becomes covered with a white efflorescence which is composed of crystals of leucin and tyrosin.

On section of the organ the surface is seen to be of a bright yellow colour. Usually in addition to the more general yellow atrophy there are areas of red atrophy. As a rule, there is more of the yellow change, but in some rare examples of what have been called acute red atrophy, diffuse red atrophy greatly predominates or is universal.

In the red areas the degenerative change is of oldest duration, while in the yellow areas it is more recent. The longer, therefore, the patient lives, the greater will be the extent of the red change found after death. The only exception to this general statement is that in prolonged cases, where compensatory hyperplasia has taken place, there may be nodular masses composed of proliferating liver cells which may be yellow or green and contrast with the surrounding red atrophy.

In the areas of red atrophy absorption of the necrotic and degenerated cells and of fat has taken place, and the only tissue left is the fibrous matrix and the capillaries which account for the red colour. Red atrophy is thus a further stage of the yellow atrophy and not an independent change. The areas of red atrophy are sunken and depressed below the level of the yellow areas. It is often more marked in the left than in the right lobe.

The outlines of the lobules are lost in the red areas and with difficulty, if at all, discernible in the yellow areas; if visible, they are much smaller than in health. The gall-bladder contains bile, often thick from mucus, but the larger bile-ducts often show only mucus. Budd* describes a case in which the bile was markedly acid.

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* Compare Trans. Path. Soc., vol. xliii, p. 83.

† Cayley, W.: Path. Trans., vol. xxxiv, p. 127.

‡ MacCallum, W. G.: Johns Hopkins Hosp. Reports, vol. x, p. 375, 1902.

The amount of fat which can be extracted from the liver is increased by about 5 per cent. above the normal, but this is far below the amount of fat which can be obtained from the liver in acute phosphorus poisoning. Possibly the fat is absorbed in acute atrophy, while in phosphorus poisoning this does not occur. But however this may be, the difference in the amount of fat is a point of distinction between the two conditions.

Alonzo Taylor † found no more fat in the liver of a case of acute atrophy than in a normal liver, but he found excess of a free fatty acid, and albumose, leucin, and asparaginic acid.

A scraping of the fresh section shows under the microscope blood-corpuscles, degenerated liver cells, and crystals of leucin, tyrosin, and xanthin. Leucin and tyrosin may be found in the blood of the veins of the liver, in the kidneys, and in the spirit in which portions of the liver have been preserved. In the alcoholic extract of the liver of acute yellow atrophy that had been kept for two years Delépine ‡ found Charcot-Leyden crystals.

Crystals of leucin and tyrosin may be seen in fresh sections, but for any satisfactory examination of the histological condition of the liver properly hardened sections are necessary. Little reliable information can be obtained from fresh sections made by the freezing method. It is, indeed, a matter of ordinary experience that fresh sections exaggerate existing disorganization of the liver. The liver, especially from a septic case, if allowed to decompose a little and then examined by means of fresh sections, shows much more apparent change in destruction of liver cells than a hardened section of the same specimen.

Histologically, the appearances vary very greatly, not only in different parts of the organ, such as the areas attacked by the yellow and by the red atrophic change respectively, but in different microscopic fields of the same section. It will be well to describe the slighter changes first and then to pass to the more advanced stages. The liver cells may show considerable fatty change, and in some parts of the liver this may be the chief alteration. In other parts the liver cells are granular, bile-stained, and show fragmentary degeneration of the nuclei, which stain badly. Hæmorrhages occur between the degenerated liver cells, and as the cells begin to undergo a further stage of necrosis, they cease to stain. These changes begin and are most marked at the periphery of the lobules, and pass in towards the intralobular vein. The small bile-ducts are in a condition of cholangitis; there is proliferation of the epithelial cells, which are discharged into the lumen of the duct and by obstruction cause jaundice. Later, necrosis of the cells lining the small ducts occurs. Proliferative changes in the interlobular bile-ducts lead to the production of columns of cells which pass into the lobules and may be regarded as an attempt at compensatory hyperplasia. In some sections the process of regeneration can be seen to be commencing in the liver cells, which are collected into solid columns, so as to imitate a primitive tubular liver. These cellular strands are separated from each other by fibrillar tissue, capillaries, or the débris of the degenerated lobule. The liver cells may be much larger than natural, contain several nuclei, and may give the impression of being made up of several liver cells which have run together. (*Vide* Fig. 72.)

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* Budd: Diseases of the Liver, p. 264, 1857.
† Alonzo Taylor: Journ. Med. Research, vol. viii, p. 424.
‡ Delépine, S.: Trans. Path. Soc., vol. xlii, p. 458.

In the more advanced stages—that is, in the areas of red atrophy—the cells of the lobules have completely disappeared as the result of very acute necrotic changes, and nothing can be seen except the skeleton of the lobules, formed of the fibrillar vascular connective tissue, enclosing a few nuclei and red blood-corpuscles. Sometimes the necrosis is so complete and widespread that it is difficult to recognise the tissue as liver or to make out the topography of the section. There is often, but not always, evidence of inflammatory reaction in the connective tissue of the liver and signs of compensatory changes in the remaining liver cells.

Thus there may be a small-cell infiltration starting from the portal spaces and spreading into the peripheral parts of the lobules; a similar small-cell infiltration may also be seen around the central venula of the lobules.

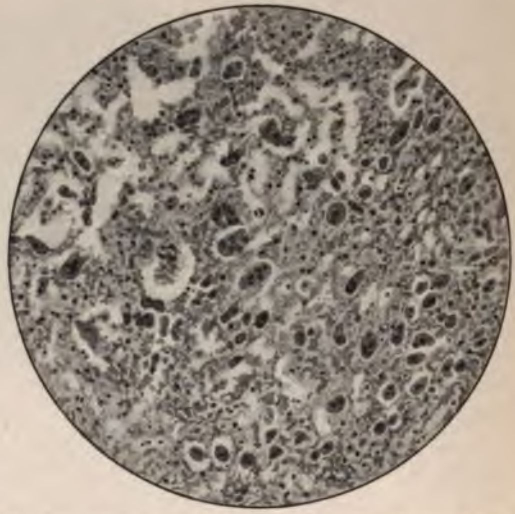

FIG. 72.—DRAWING OF MICROSCOPIC SECTION OF THE LIVER IN ACUTE YELLOW ATROPHY, SHOWING ACUTE DEGENERATIVE CHANGES IN THE LIVER CELLS.

Many of the cells are destroyed, the nuclei of some only remaining in the débris. There are, in addition, groups of liver cells and some with two or more nuclei—evidence of regeneration. × 140.

In chronic cases where there has been prolongation of life and an approach towards recovery, fibrosis, often intimate and resembling pericellular cirrhosis, may be found. It is, indeed, impossible to draw a reliable distinction between prolonged cases of acute yellow atrophy of the liver and acute cirrhosis. The proliferative changes in the interlobular bile-ducts will be described in the next paragraph on the regenerative changes.

Regenerative Changes.—Cases of acute yellow atrophy which do not run a very acute course show changes in the small bile-ducts and liver cells which may be regarded as regenerative and compensatory in character. These changes have been specially studied by Marchand *

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* Marchand: Ziegler's Beiträge, Bd. xvii, S. 206, 1895.

Meder,[*] Stroebe,[†] Barbacci,[‡] Ibrahim,[§] and W. G. MacCallum.[‖] The liver cells in the early stages of regeneration show mitotic figures and later hyperplasia, so that columns of liver cells are formed resembling a tubular formation; the liver cells may become much enlarged, especially around the intralobular vein, and may contain several nuclei. Sometimes this compensatory hyperplasia occurs only in one-half of a lobule, the liver cells in the remainder having been too much necrosed to undergo any compensatory hyperplasia; in this event the intralobular vein may appear at the margin of the fresh mass of liver cells. This method of regeneration of the liver cells leads to the production of hyperplastic or "adenomatous" nodules in the liver, which project above the surface of the surrounding parts. In cases where the liver cells have been completely destroyed, regeneration is brought about in another way. As a result of proliferation of the interlobular bile-ducts blind bile-ducts work their way into the degenerated lobule. The cells forming these projections increase in size and become like liver cells. The terminal cells in the invading masses of cells show karyokinetic figures and are evidently proliferating. Stroebe and MacCallum have specially insisted on these points and are opposed to Marchand's earlier view that these columns of cells are derived from apposition of degenerating liver cells.

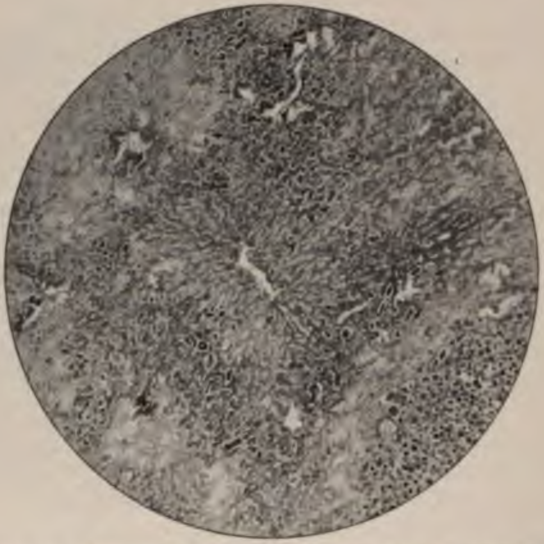

FIG. 73.—DRAWING OF A MICROSCOPIC SECTION OF ACUTE YELLOW ATROPHY OF THE LIVER, SHOWING EXTENSIVE NECROSIS OF THE LIVER CELLS.

Around the periphery of the lobules there are small-cell infiltration and groups of liver cells. × 30.

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[*] Meder: Ziegler's Beiträge, Bd. xvii, S. 143.

[†] Stroebe: Ziegler's Beiträge, Bd. xxi, S. 379, 1897.

[‡] Barbacci: Ziegler's Beiträge, Bd. xxx, S. 49, 1901.

[§] Ibrahim: München. med. Wochen., 1901.

[‖] MacCallum, W. G.: Johns Hopkins Hosp. Reports, vol. x, p 379, 1902.

To sum up, regeneration occurs in two ways: (i) From hyperplasia of pre-existing liver cells, and (ii) from hyperplasia of the interlobular bile-ducts by means of which cells approaching liver cells are produced.

Micro-organisms have been found in some cases, but not in others, and no definite causal connexion can be said to exist between any micro-organism and the changes found.

The colon bacillus, though often found after death, can hardly be regarded as the causal agent, as there may easily be postmortem invasion of the organ. Streptococci, staphylococci, pneumococci, have also been reported in some cases.

Probably several different kinds of micro-organisms, as well as several poisons, are capable of producing the acute inflammatory and degenerative changes characteristic of acute yellow atrophy of the liver.

The kidneys are swollen, soft, bile-stained, and show small hæmorrhages. Microscopically the epithelium of the tubules shows degeneration.

The spleen is often softened, as in infective disease, and often enlarged.

In 71 cases Wickham Legg found the spleen larger than natural in 43. He quotes Liebermeister's statistics of 87 cases, in 56 of which the spleen was enlarged.

The heart is softened and swollen and shows cloudy swelling. The blood, as in other toxic and septic conditions, stains the walls of the vessels and coagulates imperfectly. Hæmorrhages are found scattered through the body on the cutaneous, mucous, and serous surfaces. Meningeal and cerebral (Politzer,* Lafitte †) hæmorrhages have been known to occur. Toxic changes in the vessel walls allow extravasation to take place. Brunton and Tunnicliffe point out that viperine poison has the same effect when applied locally to the mesentery of a frog.

The gastro-intestinal tract shows evidences of catarrhal inflammation and patchy hæmorrhage, or small areas of necrosis may be found. Altered blood may be found in the stomach and intestines. A slight amount of ascitic fluid in the peritoneum is not uncommon.

Pancreas.—Degenerative changes in the acini of the gland, the islands of Langerhans being unaffected, have been described by Sacquépée,‡ who lays some stress on this since the pancreatic juice has been found to have the power of destroying the toxines of diphtheria, tetanus, etc.

Changes in the Central Nervous System.—In addition to meningeal and cerebral hæmorrhages already referred to, degenerative changes, analogous to the toxic changes seen in a more chronic form in combined sclerosis and in grave anæmia, have been described by Goldscheider and Moxter.§

PATHOGENY.

The essential factor is a very acute necrotic degeneration of the liver cells resembling that produced by bacterial toxines, with evidences of inflammation in the supporting fibrous tissue of the organ. The condition is a very acute hepatitis; comparatively chronic or protracted cases have been regarded as acute cirrhosis. It is analogous to, but more advanced than, the toxic changes seen in the liver in phosphorus, iodoform, or arsenic poisoning, or in lupinosis.

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* Politzer: Jahrb. f. Kinderheilk., 1860.

† Lafitte: Bull. Soc. Anat. Paris, 1891.

‡ Sacquépée: Archiv. de Méd. Expériment. et d'Anatomie path., t. xiv, p. 485. July, 1902.

§ Goldscheider and Moxter: Fortschritt. der Med., 1897, No. 14.

In Germany many sheep die with jaundice, hæmorrhages, delirium, and acute yellow atrophy of the liver as a result of eating certain lupins. This disease,—lupinosis,—which is not met with in man, is thought to be due to a poison—ictrogen or lupinotoxin—produced by the agency of fungi in the husks of the seeds.*

In the vomit of a fatal case of acute yellow atrophy Brunton and Tunnicliffe found a body which had a poisonous effect on guinea-pigs and was thought to be a substitute, in all probability a methylated diamine. In some cases the poisons may be produced in the alimentary canal, with or without the help of special micro-organisms. Brunton and Tunnicliffe compare the symptoms in acute yellow atrophy with those induced by some viperine venoms.

Quincke † has suggested that acute yellow atrophy may be due to obstruction at the biliary papilla, allowing the pancreatic juice to digest the liver. There is as yet no proof of this theory, which is exactly the converse of Opie's explanation of hæmorrhagic pancreatitis as due to the flow of bile into the pancreatic duct.

Flexner ‡ suggests that the lesions may be due to the autolytic action of intracellular ferments produced by some unknown agency.

As already pointed out, it is probable that a number of poisons or micro-organisms may give rise to acute yellow atrophy. At present it is not known where they are produced. But whether taken by the mouth, formed in the alimentary tract, in the liver itself, or elsewhere in the body, the liver suffers as a whole. In some cases the liver may be primarily involved, the changes elsewhere in the body being secondary, while in other instances the hepatic manifestations may be merely the local result of a general hæmic infection or intoxication.

CLINICAL PICTURE.

Course.—The disease may be divided into two stages. The first, which usually lasts five or six days, but may be prolonged for many weeks, comes on either like catarrhal jaundice with gastro-intestinal disturbance followed by jaundice, or, more gradually, with malaise. During this stage there is nothing to distinguish it from ordinary jaundice due to gastro-intestinal catarrh. After lasting for a varying time, the first stage is succeeded by the second, in which the patient passes into a "typhoid" state and develops nervous symptoms which are of the gravest significance and should at once suggest the probability of acute yellow atrophy. This stage hardly ever lasts more than a week and is usually limited to three days.

Duration.—More than half the cases, as shown by Thierfelder and

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* *Vide* Brunton and Tunnicliffe: St. Bart.'s Hosp. Reports, vol. xxxii, p. 425, 1896.

† Quincke: In Nothnagel's Encyclopædia of Practical Medicine, Diseases of the Liver, p. 642. American translation, edited by F. A. Packard, 1903.

‡ American Jour. Med. Sciences, Aug., 1903.

Hunter's statistics, run their course within two weeks. Cases, however, certainly occur in which the disease is spread over many weeks or even months. The disease has been divided into acute, subacute, and protracted cases, according to their duration and severity. The prolonged cases may resemble cases of obstinate catarrhal jaundice until the nervous symptoms develop, the long course of the disease being due to prolongation of the earlier or first stage. But in rare instances partial recovery may occur after acute symptoms have appeared, the patient remaining jaundiced.

Onset and First Stage.—As already mentioned, the onset may be that of ordinary catarrhal jaundice; in a minority, about one-third, of the cases the patient suffers from indefinite illness and malaise for some time before jaundice makes its appearance. As a rule, during the first stage there is little or nothing to distinguish the disease from ordinary catarrhal jaundice. It is true there is generally some rise of temperature, but this is often seen in benignant infectious jaundice and is not enough to justify a gloomy prognosis. Malaise, vomiting, constipation, bilious urine, and not uncommonly muscular pains are present.

Jaundice is usually the first objective sign. Its intensity varies in different cases: it may gradually become more marked, or it may, in cases that are prolonged, first fade and then become more intense before death. In some instances it may be less marked at the termination than earlier in the course of the disease. It is due to obstruction in the smaller bile-ducts, the result of inflammatory lesions in their walls produced by the same poison that is responsible for the acute degenerative changes in the liver cells. In some exceptional cases of acute yellow atrophy there is no jaundice.

This was so in a case, subsequently published by Sir T. L. Brunton and Dr. Tunnicliffe,* which was under my care when I was House Physician at St. Bartholomew's Hospital in 1889. A case of acute atrophy without jaundice was also described by Le Roy.†

In the following case, where there was no jaundice, the liver had the microscopic appearances of acute yellow atrophy: A woman aged thirty years, never strong, had slight hæmatemesis two years before, from which she recovered. On Dec. 9, 1897, she suddenly felt pain and subsequently vomited a little blood; next day the liver dulness was found to be diminished; slight hæmatemesis recurred on December 10th and 11th, and melæna on December 12th, 13th, 14th; after this date the motions, always offensive, became clay coloured. The patient got weaker, drowsy, and died on December 28th. There was never any jaundice. The urine was not tested for leucin and tyrosin. The temperature was generally between 99° and 100°, going up on two occasions to 101°, and was often below normal. At the postmortem the liver was very small, pale, firm to the touch and to the knife. The surface was smooth and of lightish yellow with patches of slate colour; the edges were remarkably thin. Gall-bladder was full of dark bile. Kidneys firm and pale. Stomach showed numerous submucous hæmorrhages, especially at the cardiac end.

Dr. E. T. Wilson, of Cheltenham, kindly sent me the liver and notes of the case. Microscopic examination showed the lesions of acute yellow atrophy.

The Second Stage.—The onset of the second stage is very definite, and is marked by a pronounced change for the worse in the general condition and especially by the appearance of nervous symptoms. Headache appears, or if present before, becomes intense. Intolerance of light is often complained of; the mental processes are affected; there are restlessness, delirium, and the patient may scream and become very violent. Twitching of the muscles often occurs, and general convulsions may supervene. Transient paralyses, such as squint, are sometimes noted. Apart from the presence of jaundice, the clinical manifestations may very closely resemble those of meningitis. The nervous manifestations tend to pass into coma, in which the patient finally dies.

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* Burnton and Tunnicliffe: St. Bartholomew's Hosp. Reports, vol. xxxii, p. 436, 1896.

† Le Roy: Lancet, 1885, vol. ii, p. 155.

With the onset of the grave nervous symptoms vomiting becomes urgent, and the vomited matters often contain altered blood. The tongue is usually dry, brown, and tremulous, and the teeth become coated with sordes. Dilatation of the pupils has been regarded as an important sign, and has been so extreme as to suggest belladonna poisoning. The pulse quickens and becomes feeble and of low tension. The respiratory rate tends to be increased or to become irregular and finally stertorous. The temperature varies, but is more often depressed than raised, but it may rise just before death. The presence or absence of fever has theoretically been correlated by Hanot * with different microbic poisons, infection with the colon bacillus leading, like phosphorus poisoning, to a depressed temperature, while streptococcal and staphylococcal infections are associated with pyrexia. Occasionally a red rash appears on the skin. Petechiæ and hæmorrhages occur under the skin, and blood may be passed in the motions; occasionally epistaxis and hæmaturia are observed, and in women metrorrhagia. Pregnant women abort. The fæces may be darkened by blood so as to resemble bile; in the later stage it is improbable that bile passes into the duodenum, inasmuch as after death the bile-ducts contain nothing but mucus. But as constipation exists throughout the disease, some of the fæces may contain bile excreted into the bowel at a very early stage of the disease. The dejecta are often extremely offensive. Diarrhœa is exceptional.

Liver Dulness.—At the onset of grave symptoms the liver may or may not be found to be enlarged. Temporary enlargement very probably occurs, though it is not made out in all cases. The increased size in the early stages may, of course, be due to some old-standing change, but this is not the case in most instances. Whether preliminary hepatic enlargement is made out or not, percussion soon shows diminution of the liver dulness, which may progress until it completely disappears. Entire absence of the liver dulness is due to the atrophied and flabby organ falling away from the abdominal walls and allowing intestinal coils to take its place.

In a very exceptional case recorded by Gerhardt † the hepatic dulness did not diminish, although the liver was markedly atrophied, weighing only twenty-nine ounces. This was explained by the fact that the liver was firmly adherent to the anterior abdominal wall.

Flatulent distension of the intestines occurs and gives rise to difficulty in estimating the size of the liver. As mentioned above, coils of intestine may pass between the abdominal wall and the liver and entirely obliterate the hepatic dulness. The liver is often tender. In 100 cases collected by Legg * this was definitely noted in 35.

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* Hanot, V.: Archiv. général. de Méd., 1896, tome clxxvii, p. 77.
† Gerhardt: Zeitschrift f. klin. Med., Bd. xxi, 1892.

Enlargement of the spleen has been occasionally noted. Ascites, though present in some cases after death, is masked by flatulence and is hardly ever detected during life.

There is no very special feature about *the blood.* The number of red blood-corpuscles has been found to be normal or to be somewhat increased in number, and a very moderate leucocytosis has been observed (Cabot Ewing †). Bacteriological examination of the blood has been negative in some instances, while in others the colon bacillus has been found (Vincent ‡).

Urine.—The amount is somewhat diminished; it is high-coloured from the presence of bile-pigment, and possibly in some instances from excess of urobilin. From degeneration of the renal cells albumin and casts are frequently present in the urine. Albumosuria is sometimes observed, and it is not improbable that the albumose is directly provided by destruction of the liver cells.

There is no glycosuria. This is a remarkable fact, and clearly shows that glycosuria is not of any value as a sign of hepatic inadequacy. Patients with acute atrophy are not likely to take much sugar, but it is very striking that sugar is practically never found in the urine. The question of glycosuria in liver disease is referred to on p. 232 (Cirrhosis of Liver).

The amount of urea is very greatly diminished, and may only be present in fractional amounts. Corresponding to the diminution in urea there is an increase in the percentage of nitrogen present as ammonia in the urine. It may increase from the normal 2 to 5 per cent. up to 17 per cent. (Herter §). The diminution in the urea is probably partly due to the liver cells failing to manufacture urea from ammonia, but it may also be in part due to organic acids seizing on the ammonia and thus preventing the formation of urea out of the basic ammonia.

Leucin and tyrosin, to which great importance has been attached as replacing urea, are sometimes present in such quantities that they are spontaneously precipitated from the urine. In many cases, however, the urine must be concentrated by evaporation in order to demonstrate them. Leucin appears in the form of rounded discs, while the crystals of tyrosin are needle-shaped. Leucin and tyrosin are not invariably present in the urine; they may be absent in cases where the liver is found to contain them, and one may be found in the urine without the other. Further than this they have been known to occur in the urine in conditions other than acute yellow atrophy; thus they have been observed in some cases of erysipelas, typhoid, variola, in some obscure febrile conditions, and leukæmia. Their presence in the urine, therefore, is not pathognomonic of acute yellow atrophy, and their absence does not exclude that disease.

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* Legg, W.: Bile, Jaundice, and Bilious Diseases, p. 465.

† Ewing: Clinical Pathology of the Blood, p. 341.

‡ Vincent: La Semaine Médical, 1893, p. 228.

§ Herter, C. A.: Lectures on Chemical Pathology, p. 344.

It was formerly assumed that the presence of leucin and tyrosin was due to the degenerated liver cells failing to transform these bodies into urea. This explanation is probably incorrect, for in cases where the liver has been excluded from the circulation by ligature of the portal vein and the hepatic artery, leucin and tyrosin do not appear in the urine. (Minkowski.) It appears more probable that the leucin and tyrosin are derived from the liver cells themselves as a result of their extensive destruction. This view is supported by the fact that leucin and tyrosin are found to result from autolysis, or the spontaneous digestion by intra-cellular ferments of other organs, *e. g.*, a pneumonic lung or pus.

Uric acid may be present in normal or even in increased quantities; the destructive metabolism in acute yellow atrophy explains this curious fact.

Termination.—The "typhoid" state deepens into coma and absolute unconsciousness, with stertorous breathing and incontinence of urine and fæces.

DIAGNOSIS.

Jaundice with severe constitutional and cerebral symptoms and diminution in the liver dulness are the main data on which the diagnosis is made.

Differential Diagnosis.—*From Phosphorus and Allied Forms of Poisoning.*—The absence of any evidence that phosphorus or other poison has been taken or vomited is, of course, important. The progressive diminution in the hepatic dulness and the diminution in the amount of urea in the urine are strongly in favour of acute yellow atrophy. The presence of leucin and tyrosin is not conclusive, as they may be absent, on the one hand, in acute atrophy, and, on the other hand, be present in phosphorus poisoning and in other conditions, such as typhoid fever, erysipelas, and even occasionally in leukæmia. In phosphorus poisoning there is an interval between the severe symptoms, due to its irritant action and the onset of jaundice with severe constitutional symptoms; while there is no such interval between the first and second stages of acute yellow atrophy. There is more gastric irritation in phosphorus poisoning.

From cases of *icterus gravis* the chief distinction is the size of the liver—diminished in acute yellow atrophy and not in icterus gravis. From severe cases of acute infectious jaundice the diagnosis is very difficult; in fact, the two conditions run into each other; those that recover are likely to be spoken of as infectious jaundice, and those that prove fatal as acute yellow atrophy. According to Osler,* cases of infective endocarditis have been mistaken for acute yellow atrophy. Hypertrophic biliary cirrhosis is not likely to be confused with acute atrophy, as the course of the disease is very chronic and the liver is greatly enlarged.

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*Osler, W.: Principles and Practice of Medicine, p. 704, 3d ed.

PROGNOSIS.

When the disease has fully declared itself, the prognosis is most gloomy; in fact, doubt will always arise as to the nature of cases that recover, and where an opportunity for examining the liver is not provided, by death later. Some of the cases, of which a good number are on record, may have been examples of infective jaundice or Weil's disease of a severe character, or of some other form of acute hepatitis.

I have had such a case under my own care where the diagnosis of acute atrophy and death, the patient being in a condition of coma, seemed equally certain, but where recovery followed. Fagge [*] refers to a case where a subsequent postmortem showed the changes of acute yellow atrophy in a patient who recovered from the acute symptoms.

Although doubt may arise as to the real nature of the lesion in the cases that recover after manifesting the characteristic symptoms, there are ample grounds for the statement that this does occur.

In 1897 Wickham Legg [†] gave a list of 28 cases of reputed recoveries from acute yellow atrophy. In 1892 Wirsing [‡] could only collect 15 cases, not associated with syphilis, of recovery.

Recovery must depend on the compensatory power of the body and especially of the liver cells. Nodular hyperplasia of the liver has been described in cases surviving for six months (Marchand [§]), a year and a half (Barbacci [||]), a year and three-quarters (Steinhaus [**]), and two years (Stroebe [††]). But the symptoms may recur and prove fatal from degenerative changes attacking the areas of compensatory hyperplasia. This occurred in a case investigated by Professor Delépine, which, by his kindness, is referred to (p. 115) under the heading of Acute Hepatitis.

As in all forms of liver disease, the state of the kidneys is of importance. If they were previously healthy, the excretion of poisons due to the acute hepatic inadequacy will diminish the intensity of the toxæmia; but even with kidneys previously intact the outlook is very dismal, since the renal epithelium is affected by the poisons reaching them by the circulation and undergoes acute degeneration.

TREATMENT.

There is no means known of curing the disease; theoretically, free purgation in the early stages of the disease, to eliminate the toxines before their degenerative effects have been produced, might be recommended. Intravenous or subcutaneous transfusion with saline solution should be employed, as in other toxæmic states.

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[*] Fagge, Hilton: Principles and Practice of Medicine, edited by Pye Smith, 3d ed., vol. ii, p. 377.

[†] J. Wickham Legg: Bile, Jaundice, and Bilious Diseases, p. 676.

[‡] Wirsing: Inaug. Disser., Würzburg. Quoted by Albu, Deutsche med. Wochen., 1901, S. 216.

[§] Marchand: Ziegler's Beiträge, Bd. xvii, S. 206.

[||] Barbacci: Ziegler's Beiträge, Bd. xxx, S. 49.

[**] Steinhaus: Prag. med. Wochen., 1903, S. 323.

[††] Stroebe: Ziegler's Beiträge, Bd. xxi, S. 379.

Lenez and Schneider[*] have reported cases where recovery followed repeated transfusions.

Intestinal antiseptics, such as minute doses of calomel, salicylate of bismuth, salol, and β-naphthol, to reduce auto-intoxication as far as possible, may be given. The excretion of the kidneys should be increased by the administration of citrate of caffeine and free draughts of water. Milk diet only should be given. Vomiting may be met by bismuth, dilute hydrocyanic acid, bimeconate of morphine, and effervescing mixtures.

JAUNDICE OF PHOSPHORUS POISONING.

Incidence.—Acute phosphorus poisoning is rare in this country; in the ten years ending 1892 there were 147 fatal cases in England and Wales. (W. Blythe.[†]) It is commoner in Vienna, and is said to be a means of committing suicide in prostitutes and unmarried girls who are pregnant, its use being perhaps associated with its reputation as an aphrodisiac. When taken with suicidal intent, an emulsion of the heads of lucifer matches or of rat paste has been employed. When accidental poisoning occurs, rat paste taken under the impression that it was something else may be the cause, but it may be due to eating the flesh of animals, especially poultry, which have died from eating vermin poisoned by phosphorus (Poore [‡]), or even from the application of phosphorescent paste to the skin. In some instances it has followed the medicinal use of phosphorus. It has been thought that some cases of acute yellow atrophy are in reality the results of undetected poisoning. Results resembling phosphorus poisoning may be due to iodoform, arsenic, and antimony.

Morbid Anatomy.—The liver is, as a rule, much larger than natural, firm but friable, and of a pale yellow colour. In a few cases the liver has presented exactly the features of acute yellow atrophy, but this is exceptional, and the change in the liver is essentially one of increase in size due to acute fatty metamorphosis, and resembles that of iodoform poisoning. It is said that if life is sufficiently prolonged, the liver diminishes in size from absorption of the fat and so comes to be in the same condition as in acute yellow atrophy. Under the capsule and on section the yellow, buff aspect of the liver substance shows here and there reddish spots due to hæmorrhage, which stand up against the bile-stained liver substance.

In dogs poisoned by phosphorus there is a large quantity of fat in the liver, and the nuclei of the liver cells show fragmentation. There is, however, no fat, or almost none, in the myocardium, none in the voluntary muscles, and only a little in the kidneys. (Ray, McDermott, and Lusk.[§])

Microscopically the liver cells show cloudy swelling and very advanced fatty metamorphosis. The cells in parts of the lobules may contain granules of bile-pigment. Leucin and tyrosin may also be found in the liver. There is sometimes slight proliferation of the connective-tissue elements of the portal spaces, and in cases that recover some cirrhosis probably develops. The small bile-capillaries are blocked and obstructed (Eppinger *), and thus account for the jaundice.

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[*] Lenez et Schneider: Arch. de Méd. et Pharm. mil., Paris, 1900, tome xxxv, p. 66. Schneider, ibid., 1903, tome xli, p. 329.

[†] Blythe, W.: Poisons, p. 213, 1895.

[‡] Poore, G. V.: Nervous Affections of the Hand and Other Studies, p. 155.

[§] Ray, McDermott, and Lusk: American Journ. of Physiology, vol. iii, p. 139, Oct., 1899.

The heart and kidneys usually, but not always, show advanced fatty change; the heart may be so soft as to be readily perforated by the fingers during its examination. The voluntary muscles also undergo fatty change. The spleen may be much enlarged. Hæmorrhages are found scattered throughout the body.

Pathogeny.—The destruction of the liver substance leads to hepatic inadequacy and so to a general toxæmia, poisons which should have been arrested in the liver passing into the general circulation. It is thought that there is an acid intoxication due to the presence of sarcolactic acid in the blood.

Clinical Manifestations.—The symptoms due to the irritating effect of phosphorus on the gastric mucous membrane come on in from a few minutes to three hours after taking the poison. With phosphorated oil or phosphorus in a soluble state the ill effects are soon manifest, while if the poison was taken in a solid form, the onset is delayed.

There is gastric pain, followed by vomiting, which greatly interferes with antidotal treatment and feeding and may be so constant as to lead to dangerous collapse. The vomited matters and eructations may be luminous in the dark, and from the presence of blood, dark and grumous. There are usually intense thirst and tenderness over the stomach and liver, but no hepatic enlargement at this stage. The patient may die from collapse; if this does not occur and efficient treatment is carried out, permanent recovery may follow, but in a considerable number of cases there is a temporary improvement succeeded by the return of grave symptoms due to the toxic effects of the absorbed poison on the liver and other internal organs. These severe symptoms usually begin about four days after the poison was taken; they may arise sooner, or, on the other hand, be delayed for two, three, or even six weeks, as in S. West's † case.

The scene reopens with jaundice and recurrence of vomiting of dark, grumous matters, followed by great prostration, ending in coma and death, usually on the fifth or sixth day from the time the phosphorus was taken, and after a day or two of grave constitutional symptoms. Hæmorrhages into the skin and from mucous surfaces are a constant feature of the disease, but are not so marked as in deep jaundice due to other causes. Jaundice is by no means a constant symptom, and does not, when present, bear any relation to the severity of the changes taking place in the liver. From experiments on animals and from observations on man (Eppinger ‡) there is reason to believe that, as in acute yellow atrophy, the jaundice is obstructive and due to inflammation of and stagnation of viscid bile in the smaller ducts. The temperature is usually below normal. The liver is enlarged and tender; the spleen is also enlarged, and the abdomen may become distended. The most marked difference between this stage of phosphorus poisoning and acute yellow atrophy is in the size of the liver. But in exceptional cases of phosphorus poisoning the liver is not enlarged, and in the early stages of some examples of acute yellow atrophy it is enlarged, so that the clinical resemblance between the two affections may sometimes be very close.

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* Eppinger: Ziegler's Beiträge, Bd. xxxiii, S. 123, 1903.
† West, S.: Lancet, 1893, vol. i, p. 245.
‡ Eppinger: Ziegler's Beiträge, Bd. xxxiii, S. 123, 1903.

There is an increase in the number of the red blood-corpuscles (v. Jaksch *), and occasionally there is leucocytosis.

The *urine* is somewhat diminished in quantity, but never suppressed; it is high coloured and of rather high specific gravity. It may contain albumin, blood, and casts. Albumosuria may also be present, the albumose being probably the direct product of destructive changes in the liver cells. There are generally bile-pigments and bile acids, while sarcolactic acid, united to ammonia, is frequently present; it is not, however, always present, as shown by Münzer's careful observations. It was formerly said that leucin and tyrosin were not present in the urine, and stress was laid on this in the diagnosis from acute yellow atrophy; it is now known that leucin and tyrosin may be present in the urine in phosphorus poisoning, but are far from being constantly found. Leucin is less frequently found than tyrosin.

The presence of leucin and tyrosin in the urine is due, like the albumosuria, to destructive changes in the protoplasm of the liver cells. That it is not, as has often been thought, due to failure on the part of the liver to transform leucin and tyrosin into urea is shown by the fact that the experimental exclusion from the circulation of the liver in geese by ligature of the portal vein and hepatic artery does not lead to the appearance of leucin and tyrosin in the urine. The amount of urea was formerly thought to be greatly diminished; it now appears that though, in common with the total nitrogen excretion, it is diminished in the early stages when all food is refused by the stomach, it is absolutely increased in the later stages as a result of increased metabolism. Experimentally it has been shown that the rise in the proteid metabolism in phosphorus poisoning is only equalled by that in phloridzin diabetes.

The proportion of the urinary nitrogen excreted as ammonia is greatly increased: instead of the normal 2 to 5 per cent., it rises to 10 to 20 per cent. of the total nitrogen; this occurs at the same time that the amount of urea is increased. The increased amount of ammonia in the urine can be diminished by the administration of sodium bicarbonate. The explanation of this is that, owing to an increase in organic acids in the body, ammonia is utilised as a base and appears in the urine in combination with organic acids; when sodium bicarbonate is given, the ammonia is no longer utilised in this way, and it is therefore free to be converted into urea.† In other words, the presence of ammonia in the urine, though associated with changes in the liver, is not due to any failure in the hepatic cells to form urea out of ammonia, but is evidence of incipient intoxication or acidosis. Sugar is not present in the urine, though in Poore's case it was found in the urine passed shortly before death. Hunter says there are only three cases on record.

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* v. Jaksch: Deutsch. med. Wochen., 1893, S. 10.

† *Vide* Herter Lectures on Chemical Pathology, p. 347.

In 19 cases of phosphorus poisoning Frerichs * gave large quantities (200 grams) of sugar, but only obtained alimentary glycosuria in two.

Diagnosis.—The history that phosphorus has been swallowed or that symptoms justifying this conclusion have recently occurred is a most important, if not an essential, point. The presence of phosphorus in the vomit or the fact that the vomited matters are luminous in the dark of course settles the question. In the differential diagnosis from acute yellow atrophy the following points should also be borne in mind: (i) The large size of the liver. (ii) The amount of urea is not diminished except in the earliest stage. (iii) The greater prominence of gastro-intestinal symptoms.

In the absence of a reliable history great difficulty may arise in the differential diagnosis; in fact, Poore † thinks that there can be no doubt that clinically and pathologically the two conditions are indistinguishable.

Prognosis.—In cases where jaundice and enlargement of the liver come on the outlook is very grave; most cases die.

Treatment.—When the poison has been recently taken, the stomach should be emptied and washed out. As an antidote, French or old or oxidised oil of turpentine should be given every quarter of an hour for the first hour, 40 minims in an emulsion, and afterwards three or four times daily. Permanganate of potash and sanitas have also been recommended. Mucilaginous drinks should be given, but oils or fats should be avoided, as they render the phosphorus more soluble. Purgatives are advisable. When the grave constitutional symptoms have developed, no special treatment can be relied on. But it would be reasonable to give large doses of sodium bicarbonate by the mouth or by subcutaneous transfusion to counteract acidosis.

INFECTIOUS JAUNDICE.

Among the various forms of toxæmic or hæmohepatogenous jaundice there is a group which, in contradistinction to the malignant forms of toxæmic jaundice or icterus gravis, such as acute atrophy and phosphorus poisoning, is spoken of as benign infectious jaundice or merely infectious jaundice. Of this group, Weil's disease is a well-marked example. The general characters of toxæmic jaundice have already been sketched (*vide* p. 530), and it was there pointed out that the jaundice is subordinate both in degree and in importance to the constitutional symptoms of a general hæmic infection or intoxication. In many instances the primary infection constitutes a definite disease, as in the specific fevers, yellow fever, pyæmia, septicæmia, etc., but in this group of infectious jaundice, although there is a general infection, its characters are not sufficiently typical to allow of its recognition as a definite disease apart from the febrile condition and jaundice.

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* F.T . Frerichs: Ueber den Diabetes, 1884. Quoted by Williamson, Diabetes, p. 116.

† Poore, G. V.: Nervous Affections of the Hand and Other Studies, p. 155, 1897.

There are thus many examples of toxæmic jaundice of undetermined nature grouped under the heading of infectious jaundice. The more severe cases are considered in a special category under the name of Weil's disease. Among the slight forms are some cases often termed catarrhal jaundice, but presenting fever and enlargement of the liver and spleen; the onset of these cases is the same as that of catarrhal jaundice, but there are the above-mentioned additional features, which tend to show that there is not a mere local obstruction at the lower end of the bile-duct, but a more widespread infection. No doubt transitional cases between a local infection and obstruction at the lower end of the bile-duct and a more extensive obstruction of the ducts exist, and it is, therefore, convenient to speak of the cases as infectious catarrhal jaundice. It is not infrequent for epidemics of this form of jaundice to occur, and it is not always easy to be certain whether it is a mild infectious jaundice, the infection falling chiefly on the bile-ducts, or whether there is an epidemic form of gastro-intestinal catarrh in which the lower end of the bile-duct is obstructed, while the ducts remain free from more extensive infection.

The epidemic jaundice which occurred in our troops in the South African war (1899–1902) was regarded by some as infectious and by others as due to epidemic gastro-intestinal catarrh.*

WEIL'S DISEASE.

Synonyms: Infective Jaundice; "Bilious Typhoid."

In 1886 Weil † described a condition of febrile jaundice associated with nephritis and enlargement of the spleen. It occurs in epidemics, one of which had previously been described by Weiss in 1866 as infectious jaundice. The disease was called after Weil, of Heidelberg, by his compatriots, but the French school did not consider it was different from icterus gravis or infectious jaundice. This unwillingness to acknowledge it as a new disease distinct from other forms of toxæmic or infectious jaundice is shared by Hunter ‡ in his article in Allbutt's "System of Medicine."

Weil's disease is an excellent example of acute infective jaundice secondary to a hæmic infection by a proteus bacillus. The jaundice is toxæmic, and has close analogies with that induced experimentally by means of toluylendiamin. It is allied to, but less acute than, acute yellow atrophy of the liver; thus cases formerly recorded as examples of recovery from acute yellow atrophy would probably be regarded now by many as Weil's disease. Conversely, fatal cases of Weil's disease are sometimes described as acute yellow atrophy or icterus gravis.

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* *Vide* Report of the Imperial Yeomanry Hospitals in South Africa, vol. iii, p. 195.

† Weil: Deutsches Archiv f. klin. Med., Bd. xxxix, 1886.

‡ Hunter, W.: Allbutt's System, vol. iv, p. 100.

Etiology.—It usually attacks young adults, and is more frequent in males between the ages of twenty and forty years, but children are sometimes attacked. The infection is probably conveyed into the system by eating decomposed meat or drinking water which has been infected by tainted meat or by the bodies of animals dying from a similar disease. Its frequency in the German army has been referred to the consumption of rancid and improperly cooked sausages. (H. Brooks.[*]) Semmola and Geoffredi[†] quote cases where the disease appeared to be due to inhalation of sewer-gas. It is, therefore, more likely to occur in those classes of the population who are exposed to the sources of infection, such as butchers, sewermen, soldiers, etc.

Most of the cases occur in the summer months, and are met with in epidemics. It may arise repeatedly in the same place, but does not appear to be contagious.

The disease is rare in England, though some epidemics of catarrhal jaundice have been erroneously described as Weil's disease, and is usually seen in Germany, Russia, and France. Very few cases have been recorded in America (Raymond,[‡] Lamphear, H. Brooks,[§] Libman,[‖] Satterlee[**]).

Bacteriology.—Jaeger,[††] Banti,[‡‡] and others have described a proteus bacillus as the essential cause of the disease. Jaeger found the same organism (Bacillus proteus fluorescens) in ducks dying with jaundice, which frequented the water in which his patients had bathed and presumably become infected. Satterlee has given a useful table showing the characters of the bacilli found by Weil, Jaeger, Brooks, Libman, and himself.

This bacillus is found in the viscera in large numbers, and when cultivated and injected into animals, leads to acute degenerative changes in the liver and kidneys. It appears that bacilli are rarely present in the blood, and that dissemination occurs chiefly by the lymphatics. (H. Brooks.)

Morbid Anatomy.—The tissues of the body are bile-stained and show the effects of a general toxic process. The liver is either somewhat increased in size, or of the normal volume, and thus differs from the condition in acute yellow atrophy.

Hæmorrhages may be present in the skin and in the mucous and serous membranes. The spleen is swollen, enlarged, and has been seen to contain hæmorrhages. The kidneys show tubal nephritis.

There is cloudy swelling of the cells of the kidney, liver, and heart muscle, going on to the further degenerative change of fatty metamorphosis. The changes in the liver may progress further and resemble those in acute yellow atrophy; the mucous membrane of the bile-ducts becomes swollen and degenerated.

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[*] Brooks, H.: Archives of Neurology and Psychopathology, 1900, p. 344.

[†] Semmola and Geoffredi: Twentieth Century Practice, vol. ix.

[‡] Raymond: Medical Age, Detroit, Oct. 10, 1892.

[§] Brooks, H.: Archives of Neurology and Psychopathology, vol. iii, p. 343.

[‖] Libman: Philadelphia Med. Journ., 1899, p. 620.

[**] Satterlee: Medical News (N. Y.), June 6, 1903, p. 1069.

[††] Jaeger: Zeitschrift f. Hygiene, Bd. xii, S. 525.

[‡‡] Banti: Deutsche med. Wochen., 1895, S. 493.

Symptoms.—The onset is sudden and, generally speaking, resembles that of influenza. The chief symptoms are malaise, headache, fever, severe muscular pains, especially in the calves, and often more or less marked gastro-intestinal disturbance. The pulse-rate is about 120 at first, but becomes slower after the appearance of jaundice. Jaundice begins on the second or third day, is generally slight, and lasts about two weeks; the motions may be clay-coloured, but usually contain bile and are often loose. The liver becomes enlarged and tender, and a marked feature of the disease is the splenic enlargement. Fever reaching 103° to 104° F. lasts for about a week; the temperature then falls and becomes normal at about the tenth day.

Nervous symptoms are prominent; the muscular pains in the calves are severe, prostration and giddiness may be marked, and delirium is usually present. Epistaxis, purpura, and various cutaneous rashes, such as herpes, erythema, and urticaria, may be met with. A relapse may occur a week or so after the temperature has become normal; its occurrence may be suspected if, after the end of the first attack, the spleen remains enlarged. The relapse lasts about a week. Chauffard[*] describes Weil's disease as "relapsing infectious jaundice," but in Germany relapses are comparatively infrequently described; thus, in 84 cases, of which 73 were collected from German literature, Tymowski[†] found that relapses were mentioned in 19. Quincke[‡] says that a relapse occurs in 40 per cent. of the cases.

Bacteriological examination of the blood shows that it is almost always sterile, and that the proteus bacillus, described by Jäger and others, in the viscera, is not to be found in the general circulation. The blood-serum may agglutinate the Bacillus typhosus even when diluted (Eckhardt[§]).

The urine is albuminous, contains bile-pigment, casts, and sometimes blood-corpuscles and bile acids. Bacteriological examination of the urine shows that the same proteus bacillus found in the viscera is present. Bacteriuria may persist for a considerable time; in Satterlee's case, where it was still present and rendered the urine turbid a month after the disease, it may have been due to local infection of the prostate.

Diagnosis.—Fever, jaundice, enlarged spleen and liver, pains in the calves, and albuminuria occurring in epidemics, running an acute course, and ending in recovery are the characteristics of the special form of infectious jaundice called Weil's disease. Very similar forms of infectious jaundice occur and differ in some clinical features, such as the absence of albuminuria or constant association with gastro-intestinal symptoms. It is, indeed, hardly worth while separating Weil's disease from these forms of infectious jaundice.

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[*] Chauffard: Traité de Médecine (Bouchard, Brissaud), tome v, p. 98.

[†] Quoted by Chauffard, *loc. cit.*

[‡] Quincke: Diseases of Liver in Nothnagel's Encyclopædia of Practical Medicine, English translation, p. 504.

[§] Eckhardt: München. med. Wochen., Bd. xlix, S. 1129, 1902.

From ordinary *catarrhal jaundice* it is distinguished by its greater severity and by evidence of its being not a local disease limited to the bile-ducts, but a general infection, as shown by albuminuria.

From Typhoid Fever.—Griesinger originally described the disease as "bilious typhoid." Not uncommonly cases of Weil's disease occur in association with typhoid fever. Further, according to Eckhardt,* the blood-serum in Weil's disease may agglutinate typhoid bacilli in a marked manner even when diluted, and so lead to difficulty in a differential diagnosis. That Weil's disease is not modified typhoid fever seems quite clear, as the lesions of typhoid are not found in fatal cases of Weil's disease. In differentiating the two diseases clinically the onset of Weil's disease is sudden, and gradual in typhoid fever. The duration and course of Weil's disease are shorter than those of typhoid fever. Jaundice is extremely rare in typhoid fever.

The more severe examples of Weil's disease approach icterus gravis and acute yellow atrophy. The difference is one of degree, so far as our present knowledge goes.

Relapsing fever should be recognised by examination of the blood and the presence of the Spirillum Obermeieri. Mild cases of yellow fever, according to Brooks, are much the same as Weil's disease, and it is possible that not only are they both examples of toxæmic jaundice, but that the infection is the same.

The **prognosis** is fairly favourable, but convalescence may be protracted.

In the 44 cases obtained by adding Weil's, Jäger's, Haas's, and Wassilieff's figures there were only five deaths. It must be borne in mind, however, that fatal cases are very likely to be described as icterus gravis or acute yellow atrophy simply because they are fatal.

Treatment.—The patient should remain in bed until after the temperature has become normal, and should be restricted to a milk diet. All alcoholic drinks should be interdicted, and the patient should be encouraged to drink freely of water. Intestinal antiseptics, such as calomel ($\frac{1}{40}$ gr.) in minute doses, salol, salicylate of bismuth, or β-naphthol, should be given.

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* Eckhardt: München. med. Wochen., Bd. xlix, S. 1129, 1902.

DISEASES OF THE GALL-BLADDER.

ABNORMALITIES.

Complete Absence of the Gall-bladder.—This is the normal condition in the horse, mule, ass, elephant, and other animals. It is sometimes seen in man, but some of the older observations, such as those of Cholmeley,[*] Thomas,[†] were evidently on cases of obliteration of the gall-bladder due to inflammation during fœtal life, and not of genuine absence of the gall-bladder.

I have seen only one case at St. George's Hospital, in a man aged forty-nine who died from pulmonary tuberculosis; the ducts were quite normal, and there was no evidence of past inflammation or of any dilatation. This case was dissected and described by Dr. A. Latham.[‡] Thursfield showed an undoubted case at the Pathological Society on April 7, 1903.

In genuine cases the common bile-duct is sometimes dilated in some part of its course. This change has also been said to occur in some cases where the gall-bladder has been removed by the surgeon.

Crucknell's [§] case, in which the common hepatic duct was described as opening into the gall-bladder and the common bile-duct as coming off separately from the gall-bladder, so that all the bile must have passed through the "gall-bladder," was probably a case of absence of gall-bladder and dilatation and pouching of the upper end of the common bile-duct.

Double Gall-bladder.—In exceptional instances there have been two gall-bladders, each with a cystic duct.

Purser [‖] described an example in 1886 and referred to a case recorded in the Philosophical Transactions of 1693–4 in which there was a gall-bladder on the left lobe and another on the right lobe of the liver.

Malposition of the Gall-bladder.—In rare instances the gall-bladder is found to the left of the longitudinal fissure and on the under surface of the left lobe.

There is a specimen showing this in the Anatomical Museum, Cambridge, and Dévé [**] figures another example.

In cases where the left lobe is atrophied the gall-bladder appears to be attached to the left margin of the liver (*vide* Fig. 3), and may become so situated as to have its long axis at right angles to the long axis of the body.

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[*] Cholmeley: Med. Trans. Roy. Coll. Physicians, London, vol. vi, p. 50, 1820.

[†] Thomas: Medical Times, vol. xvii, p. 171, 1848.

[‡] Latham: Proc. Anat. Soc., Feb., 1898. Journ. of Anat. and Physiol., 1898.

[§] Crucknell: Trans. Path. Soc., vol. xxii, p. 163.

[‖] Purser: Trans. Acad. Med. Ireland, vol. v, Brit. Med. Journ., 1886, vol. ii, p. 1106.

[**] Dévé: Bull. Soc. Anat. Paris, 1903, p. 261.

In some instances the fundus of the gall-bladder is deeply indented into the substance of the liver, and may show through on the anterior surface of the right lobe, looking like a cyst embedded in the substance of the organ. The notch at the anterior margin of the liver is absent in these cases. In exceptional instances the posterior surface of the gall-bladder may be covered over for some distance by a bridge of liver substance and justifies the term intra-hepatic gall-bladder. (Dévé.)

Abnormalities in Size and Shape of the Gall-bladder.—Quite apart from inflammation or gall-stones the fundus of the gall-bladder, just where it projects beyond the anterior margin of the liver, may show a constriction which resembles the pathological hour-glass gall-bladder. The projecting portion of the gall-bladder may be twisted like a fish-hook (Dévé). In rare instances fat is found under the peritoneal coat of the gall-bladder; it is of no pathological importance. Subserous œdema is sometimes present in cases of ascites, in the backward pressure of heart-disease, and occasionally when there is no associated pathological change to be found.

ACUTE CHOLECYSTITIS.

Acute cholecystitis has various degrees of intensity; it may, like appendicitis, be catarrhal, suppurative, ulcerative, and phlegmonous or gangrenous, according to the virulence of the infection and the resistance of the organ. It is possible that an inflammation which at first is characterized by a serofibrinous exudation may subsequently become purulent, so that what is an acute serous cholecystitis at the outset may eventually present itself as an empyema of the gall-bladder. The causes of acute cholecystitis will first be considered generally, and then a separate description will be given of the acute catarrhal, suppurative, phlegmonous, and gangrenous forms.

CAUSES OF ACUTE CHOLECYSTITIS.

Acute inflammation of the gall-bladder is very closely bound up with the same process in the ducts, and from the point of view of causation it is rather an artificial distinction to describe these two conditions separately. Acute inflammation may begin in the ducts, as in suppurative cholangitis due to the rupture of an hydatid cyst into the ducts, and spread to the gall-bladder. In some instances an acute cholangitis may infect the gall-bladder, which eventually goes on to suppuration while the primary lesion resolves. On the other hand, acute inflammation may begin in the gall-bladder, as in typhoidal infection, and remain limited to it, or subsequently spread to the ducts.

The conditions leading to acute cholecystitis, whether suppurative or not, are: (1) *Disposing;* (2) *exciting.*

I. DISPOSING CAUSES.

The factors which reduce the resistance of the gall-bladder and render it more liable to infection and inflammation are: (*a*) A previous attack of inflammation of the gall-bladder naturally renders the organ more susceptible. Possibly the micro-organisms may remain in a latent condition and a relapse may be induced. Further, an attack of mild cholecystitis leads to the formation of calculi in the gall-bladder.

(*b*) Calculi in the gall-bladder may, by their action, render a secondary infection more easy.

(*c*) The rare occurrence of foreign bodies, such as worms, the ova of parasites, in the gall-bladder would have a similar influence to calculi in the gall-bladder.

(*d*) Any factors leading to biliary obstruction or stagnation of bile in the gall-bladder favour the multiplication of any micro-organisms which have gained entrance to the gall-bladder, inasmuch as they are not flushed out, but remain in that viscus. These factors are discussed under the heading of Gall-stones (p. 703), and include sedentary habits, obesity, abdominal tumors, pregnancy, tight lacing, and other conditions which interfere with the descent of the diaphragm.

II. DIRECT OR EXCITING CAUSES.

(*a*) Microbic infection of the gall-bladder; this is the cause of almost all the cases.

(*b*) Toxines reaching the gall-bladder and, in the absence of any micro-organisms, setting up cholecystitis. This is largely a theoretical consideration.

(*c*) Traumatism of the gall-bladder.

(**A**) **Microbic Infection.**—The infectious diseases which lead to local manifestations in the gall-bladder, by means of microbic infection, may be divided into two classes, which, however, to a certain extent, overlap: (1) General hæmic infections. (2) Diseases of the alimentary canal and the direct spread of acute inflammation from the larger bile-ducts. (*Vide* Cholangitis.)

In the first group come septicæmia, pyæmia, and influenza, while in chronic Bright's disease, where terminal infections are common, the gall-bladder might be picked out. The diseases of the alimentary canal include typhoid fever, which is of great interest, cholera (Galliard *), and other microbic infections of the bowel. Appendicitis is a probable focus from which micro-organisms may travel to the liver and the gall-bladder † and it is far from uncommon to find gall-stones (or the evidence of past cholecystitis) and appendicitis in the same individual. Influenza may also, in virtue of its gastro-intestinal form, be included under this heading.

(1) *In general hæmic infections* micro-organisms may reach the gall-bladder, being excreted into its cavity and into the bile-ducts from the branches of the hepatic artery. Acute cholecystitis may follow pneumonia and be due to infection of the gall-bladder with the Diplococcus pneumoniæ.

Acute cholecystitis apparently following influenza, but resolving, so that no proof of its nature can be obtained, is probably not very rare. Some of the cases of jaundice following influenza may show cholecystitis, as well as inflammation of the ducts.

F. A. Packard ‡ records a case of what appeared to be influenzal cholecystitis. The following case occurred at St. George's: A man aged forty was admitted under my care with the pains of influenza behind the eyes and in the limbs. He had had a sudden onset of vomiting and intense colic, like that of gall-stones. There was tenderness over the gall-bladder, which could not be felt, and the vermiform appendix, but there was no jaundice and no calculus could be found in the stools. He made a rapid recovery. The case appeared to be one of the gastro-intestinal form of influenza with cholecystitis.

In diseases of the alimentary canal the infection of the gall-bladder is due to the passage of micro-organisms, especially the colon and typhoid bacilli, from the bowel to the gall-bladder. The channel by which this infection takes place is often assumed to be one of direct extension up the common bile-duct. In the case of typhoidal cholecystitis there are grounds for doubting whether this is necessarily the case. (*Vide* p. 595.) The fact that under normal conditions the empty duodenum is sterile, or almost so, makes it probable that in the absence of duodenal inflammation micro-organisms reach the gall-bladder by the blood stream rather than by direct extension up the common bile and cystic ducts. The occurrence of influenzal cholecystitis has already been referred to. The relation of appendicitis and cholecystitis is one of considerable interest. The two conditions may coëxist. It is possible that in some cases both organs are attached by a simultaneous infection; that in others appendicitis is primary and provides an inlet for micro-organisms which set up cholecystitis (Ochsner [*]), or, lastly, that the cholecystitis is primary and the appendicitis secondary (Dieulafoy [†]). Catarrhal or suppurative cholecystitis, with or without gall-stones, may be found associated with appendicitis.

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* Galliard: La Cholera. Bibliothèque Charcot-Debove, 1894.

† *Vide* Ochsner: Philadelphia Med. Journ., Oct. 6, 1900, p. 652.

‡ Packard: Philadelphia Med. Journ., Nov. 4, 1899, p. 879.

Cholecystitis Due to Infection with Bacillus Coli.—This subject is of great importance in connexion with the production of gall-stones, and is referred to under that heading. The channels by which colon bacilli pass into the gall-bladder are probably much the same as those by which typhoid bacilli reach the gall-bladder, viz., by the blood of the portal vein. In some cases an ascending infection from the duodenum may occur. Infection of the gall-baldder may follow intestinal disorders in which the colon bacilli become virulent, or may be due to absorption of bacilli from an intestinal ulcer or possibly from an inflamed vermiform appendix.

Cholecystitis Due to Typhoidal Infection.—The clinical fact that inflammation of the gall-bladder may complicate typhoid fever has been known since Louis' and Andral's time (1826). Budd,[‡] Ayres,[§] Pepper,[‖] and other observers recorded early cases. A good résumé of the history of typhoidal cholecystitis will be found in A. L. Mason's,[**] and Camac's[††] articles.

Gilbert and Girode,[‡‡] in 1890, were the first to prove bacteriologically that suppurative cholecystitis may be due to typhoid bacilli. Since that time numerous cases confirming this discovery have been reported by Chiari [§§] and others.

Cholecystitis during or after typhoid fever need not, however, be due to typhoidal infection. Thus Cushing [‖‖] has met with five cases of post-typhoidal cholecystitis in which a pure culture of Bacillus coli was obtained. There may be a mixed infection of Bacillus coli and Bacillus typhi, as in Marsden's[*] case.

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[*] Ochsner: Philadelphia Med. Journ., Oct. 6, 1900, p. 652.

[†] Dieulafoy: La presse Médicale, June 17, 1903, p. 445

[‡] Budd: Diseases of the Liver, 2d ed., 1857, p. 195.

[§] Ayres: New York Journ. Med., 1846, vol. vii, p. 315.

[‖] Pepper, W., Sr.: American Journ. Medical Sciences, Jan., 1857.

[**] Mason, A. L.: Trans. Assoc. American Physicians, vol. xii, p. 23.

[††] Camac: American Journ. Med. Sciences, 1899, vol. cxvii, p. 275.

[‡‡] Gilbert and Girode: C. R. et Mem. de la Soc. biol. Paris, 1890, p. 756, 1890; ibid., 1893, p. 956.

[§§] Chiari: Prag. med. Wochen., 1893, No. 22. Zeitschrift f. Heilkunde, Bd. xv, S. 199.

[‖‖] Cushing: Johns Hopkins Hosp. Bulletin, May, 1898.

The incidence of cholecystitis in typhoid fever is difficult to estimate, inasmuch as the slighter cases must often escape detection. Sometimes palpation of the gall-bladder gives rise to pain but to no further symptoms, and it is impossible to speak with any certainty as to the condition of affairs. Murchison[†] and Chiari's observations are in favour of latent cholecystitis in enteric not being uncommon. Camac has collected 115 cases.

In 494 cases of enteric at Montreal tabulated by Gillies[‡] there were four examples of cholecystitis, of which one (suppurative) was fatal.

In 1016 cases of enteric fever admitted into the Imperial Yeomanry Hospitals in South Africa during the War 1900–1901 only one case of cholecystitis was sufficiently marked to require operation or to be recognised beyond any doubt.

Typhoidal cholecystitis usually occurs in young adults, but cases in girls of five and six years old have been recorded by Alexief[§] and Mason.[‖]

There is very considerable variation in the interval between the primary attack of typhoid fever and the attack of cholecystitis. It may complicate the attack or may occur as long as fourteen[**] or twenty[††] years after. In some instances there is no history of any attack of typhoid fever. (Osler,[‡‡] Cushing,[††] Richardson.[§§]) Cholecystitis complicating typhoid fever is very seldom associated with cholelithiasis, though the presence of gall-stones would dispose the gall-bladder to inflammation should enteric fever supervene. Acute cholecystitis following typhoid fever after an interval of months or years is more often associated with cholelithiasis.

In 1898 Cushing collected 6 cases of post-typhoid cholecystitis associated with gall-stones which had been operated upon and shown to contain the typhoid bacilli. In 31 cases of cholecystitis operated upon by Halsted 10 gave a history of enteric fever, the interval being from a few months to twenty years.[‖‖]

It is generally assumed that the bacilli found in the gall-bladder years after an attack of typhoid are the descendants of those that gave rise to the original illness. But it is possible that they have been subsequently derived from the alimentary canal of a person who, from a previous attack of enteric fever, is immune.

The typhoid bacilli may conceivably reach the gall-bladder by several routes, viz., by the portal vein, the hepatic artery, the common bile-duct, or possibly even through the walls of the bowel.

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[*] Marsden: Medical Chronicle, Jan., 1901, p. 269.

[†] Murchison: Continued Fevers, 3d ed., p. 634.

[‡] Gillies: Montreal Medical Journ., June, 1900.

[§] Alexief: Journ. Lietskaya Meditzina, 1896; abstract in American Journ. Med. Sciences, Oct., 1897.

[‖] Mason: Trans. Assoc. American Physicians, vol. xii, p. 23.

[**] v. Dungern: München. med. Wochen., June 29, 1897.

[††] Osler: Trans. Associat. American Physicians, vol. xii, p. 384, 1897.

[‡‡] Cushing: Bull. Johns Hopkins Hosp., May, 1898.

[§§] Richardson, M.: American Journ. Med. Sciences, June, 1898, vol. cxv, p. 648.

[‖‖] Quoted by Cushing: Johns Hopkins Hosp. Bull., May, 1898.

By the Portal Vein.—The bacilli have but a short way to travel to reach the liver by the portal vein; here they set up areas of focal necrosis, and, having thus injured the liver tissue, are able to pass into the bile-ducts.

Sherrington[*] has shown that bacilli alone, even though teeming in the blood, cannot pass through normal hepatic tissues, but that some previous damage by the toxines they produce is first necessary. Carmichael[†] has also shown that after injections of typhoid cultures into the portal vein the bile still remains sterile. It is, however, not improbable that during the course of typhoid fever the walls of the ducts or of the gall-bladder would become damaged by toxines excreted from the blood-stream and so permeable to micro-organisms, and that typhoidal infection from the portal vein may then take place.

From the Hepatic Artery.—Typhoid bacilli may also reach the liver by the hepatic artery and so be excreted into the bile-ducts and gall-bladder. Though in typhoid fever bacilli are not ordinarily present in the general circulation, they may pass out of the portal system into the circulation in a kind of wave, and then settle down in the bone-marrow, liver, and other situations, the circulation thus becoming cleared of them. This is shown by the fact that typhoid bacilli may pass into the urine. In cases of typhoidal septicæmia without intestinal ulceration the bacilli have been found in the bile. So both in ordinary typhoid fever and in typhoid septicæmia typhoid bacilli may travel by the arterial system to the liver.

By Direct Extension up the Common Bile-duct.—The motile typhoid bacilli might readily travel from the duodenum up the common bile-duct and reach the gall-bladder. The belief in an ascending infection of the gall-bladder from the duodenum is widely received. Carmichael,[‡] finding that experimental injection of various micro-organisms into the portal vein did not lead to infection of the bile, argues in favour of a direct extension up the common bile-duct.

Cushing and Livingood,[§] however, in experiments on the bacteriological condition of the duodenum, find that it is often sterile when not containing food, while the lower portion of the small intestine contains numerous micro-organisms. This would in some degree render an ascending infection of the ducts improbable. Further, if typhoidal cholecystitis were an ascending infection, it is probable that other micro-organisms, such as the Bacillus coli or streptococci, would be present, and that the culture would not be a pure one. (Cushing.[‖]) On these grounds it is unlikely that the infection in typhoidal cholecystitis is an ascending one.

It has been suggested that micro-organisms pass directly through the walls of the intestine into the peritoneal cavity and then through the walls of the gall-bladder. This may take place when both the viscera concerned are inflamed and so allow of the passage of micro-organisms through their walls; in this way a secondary infection of the gall-bladder when already inflamed may be brought about, but it is highly improbable that primary gall-bladder infection is started in this way.

Typhoid bacilli are almost constantly present in the gall-bladder in fatal cases of typhoid fever; this contrasts with the comparative infrequency of cholecystitis. Probably some additional factor, such as traumatism, previous disease, gall-stones, or extreme stagnation of bile, is necessary before the bacilli are able to set up cholecystitis.

Bacteriology of Cholecystitis.—Besides the colon and typhoid bacilli, streptococci, staphylococci, or pneumococci may give rise to cholecystitis. The Diplococcus pneumoniæ may attack the gall-bladder primarily, there being no pulmonary or other manifest lesions. According to Richardson,[**] pneumococcal cholecystitis is more acute and severe than that due to colon or typhoidal infection. Mignot[††] found that there was no remarkable anatomical difference in experimental cholecystitis due to streptococci, staphylococci, or the colon bacillus. Secondary infections may occur, so that typhoid bacilli, streptococci, staphylococci, etc., may be found together. In primary typhoidal cholecystitis the inflamed gall-bladder may become adherent to adjacent intestinal coils, and the tissues being inflamed, micro-organisms may pass from the bowel into the gall-bladder.

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[*] Sherrington: Journ. Path. and Bact., vol. i, p. 258, 1893.

[†] Carmichael: Journ. Path. and Bact., vol. viii, p. 276.

[‡] Carmichael: Journ. Path. and Bact., vol. viii, p. 276.

[§] Cushing and Livingood: Johns Hopkins Hosp. Reports, vol. ix.

[‖] Cushing: Johns Hopkins Bulletin, Nos. 101, 102, Aug.–Sept., 1899.

[**] Richardson: American Journ. Med. Sciences, June, 1898, vol. cxv, p. 637.

[††] Mignot: Thèse Paris, 1897.

Wanchscheim * records a case bearing this interpretation. In a fatal case of typhoid fever the gall-bladder contained pus and typhoid bacilli while the peritoneal lymph on the surface of the gall-bladder showed the Staphylococcus pyogenes aureus, which was regarded as a secondary infection from the walls of the intestine.

(**B**) **Toxic Cholecystitis.**—Although, practically speaking, acute cholecystitis is always due to bacterial infection of the gall-bladder, it has been shown by Claude's † experiments that bacterial poisons are capable of inducing changes allied to inflammation in the gall-bladder.

In 82 animals poisoned with abrin or with the toxines of diphtheria, tetanus, streptococci, staphylococci, Bacillus coli, and Bacillus pyocyaneus Claude found hæmorrhages into the gall-bladder in seven.

On the analogy of toluylendiamin, which sets up an inflammation of the small ducts in the liver which may spread down into the duodenum (Hunter ‡), it is reasonable to assume that toxic inflammation of the small bile-ducts in man might extend into the gall-bladder and set up acute cholecystitis. It is, however, probable that if a toxic cholecystitis occurred it would soon become infected with micro-organisms reaching the gall-bladder by the blood-stream. As the matter stands, cholecystitis due to poisons, as apart from microbic infection, is a theoretical possibility rather than an established occurrence in practice.

Traumatism, such as a fall or blow in the region of the gall-bladder, may so reduce its resistance that any micro-organisms present, which would otherwise be removed or destroyed, are enabled to gain a footing and set up inflammation. It is known, for example, that in typhoid fever the bacilli are practically always found in the gall-bladder, but that cholecystitis is comparatively infrequent. Traumatism in such cases would be a directly exciting cause of cholecystitis. A blow may set up acute inflammation in cases where a calculus is latent in the gall-bladder.

Kehr § reports the case of a doctor, who after being knocked down by a bicyclist, rapidly developed acute inflammation in a contracted gall-bladder the cystic duct of which was blocked by a single calculus.

FORMS OF ACUTE CHOLECYSTITIS.

There are several forms of acute cholecystitis. In the least severe, serous or catarrhal cholecystitis, the exudation does not contain pus. In suppurative cholecystitis the gall-bladder is the site of an acute purulent inflammation. Midway between these two, and somewhat difficult to include in either, is chronic empyema of the gall-bladder. In this condition an acute attack of inflammation is succeeded by a chronic infection of the gall-bladder which gives rise to the gradual formation of pus. This chronic suppurative cholecystitis is clinically more allied to dropsy of the gall-bladder, and is referred to again as one of the sequelæ of acute catarrhal cholecystitis. The most severe forms of acute cholecystitis are the phlegmonous and gangrenous.

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* Wanchscheim: Prag. med. Wochen., 1898.

† Claude: Bull. Soc. Anat. Paris, 1896, p. 502. Medical Week, 1897, p. 309.

‡ Hunter, W.: Trans. Path. Soc., vol. xli, p. 105.

§ Kehr: Gall-Stone Disease, p. 223, American translation.

It will be seen that these three forms, catarrhal, suppurative, and phlegmonous, constitute an ascending series in the severity of the inflammation, but that they merge into each other, and that a distinction between any two of them may be difficult.

ACUTE CATARRHAL INFECTIVE CHOLECYSTITIS.

Under this heading are included acute inflammations of the gall-bladder which stop short of the production of pus. A number of different forms of inflammation are here grouped together. In some instances there is only a serous exudation; in others it is serofibrinous or may go on to ulceration. Acute catarrhal cholecystitis is also an early stage of suppurative inflammation.

The causes of cholecystitis have already been described, and need not be recapitulated, but it may be pointed out that the less severe form (catarrhal) of acute cholecystitis may be produced by the same micro-organisms which, under more favourable conditions or when more virulent, set up suppurative inflammation; thus typhoidal infection of the gall-bladder may give rise to a simple serous cholecystitis or to a severe suppurative inflammation.

Morbid Anatomy.—The gall-bladder is distended and its walls are tense; the serous coat may be dulled from the presence of fibrin, and adherent to adjacent parts. In severe cases the coats of the gall-bladder are swollen from infiltration and softened. The mucous membrane is congested, and may be ulcerated or show a deposit of bile on its surface. The cystic duct is often closed by catarrhal swelling of its mucous membrane, or, as the result of past inflammation and ulceration due to the passage of a calculus, may be permanently obliterated. The cystic duct, however, is not necessarily closed in catarrhal cholecystitis. The contents of the gall-bladder may be practically clear and like serum when the cystic duct has been blocked for some time, or consist of serofibrinous or bile-stained, turbid fluid. There may be gall-stones or inspissated bile. The lymphatic glands in relation to the cystic and common bile-ducts are enlarged. In cases where recurrent attacks of acute cholecystitis occur the glands may become so hard as to imitate infiltration with malignant disease, when felt during an operation.

Microscopically the fibromuscular coat shows small-cell infiltration and dilatation of the blood-vessels. It is difficult to speak with any certainty about the condition of the mucous membrane, since under normal conditions the mucosa is macerated and destroyed by the bile and disappears about five hours after death. (Sudler.*) In the less ture usually remains normal. But if the inflammation is severe or extends to the ducts or to the peritoneal coat of the gall-bladder, there may be fever, sometimes of such a degree as to suggest suppuration, which, however, as shown by operation, is not present.

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* Sudler, M. T.: Proc. Assoc. American Anatomists, 1900, p. 177.

In rare instances micro-organisms absorbed from the mucous membrane of the gall-bladder may give rise to infection elsewhere, such as appendicitis (Dieulafoy *) or endocarditis (Lorrain †).

Diagnosis.—When the gall-bladder is felt as a tumor it must be distinguished from such conditions as impacted fæces in the colon, hydronephrosis or renal tumor, and floating kidney. The differential diagnosis of a distended gall-bladder from other conditions is given on page 737 (mechanical results of gall-stones).

The diagnosis from suppurative cholecystitis may present considerable difficulties; no hard-and-fast line separates the more acute cases of cholecystitis without actual pus formation from the slighter cases of suppurative cholecystitis. Acute cholecystitis may possibly be the early stage of the suppurative form. From a clinical point of view the difference between acute catarrhal and suppurative cholecystitis is one of degree, the pain, tenderness, and constitutional symptoms being much more marked in the latter.

From biliary colic, which is probably always accompanied by some inflammation of the gall-bladder, the diagnosis of acute catarrhal cholecystitis may also be difficult. The pain is more excruciating in gall-stone colic, while the signs of local mischief, such as tenderness, paralytic distension of the intestines, or a palpable tumor in the situation of the gall-bladder, are more prominent in acute cholecystitis.

The milder cases of acute cholecystitis are sometimes a secondary part of acute cholangitis, and are due to extension of the inflammatory process; in such cases the aspect of the disease is that of catarrhal jaundice, the existence of cholecystitis being determined only by tenderness over the gall-bladder, which may, perhaps, be palpably enlarged.

A mistake which is very easily made is to regard as appendicitis a case of cholecystitis. This is very likely to occur when the gall-bladder is dilated or so elongated as to reach into the right iliac fossa. In cases where the right lobe of the liver is prolonged into a Riedel's lobe, the gall-bladder may approach the anatomical situation of the vermiform appendix, and when inflamed, will imitate perityphlitis. The presence of peritoneal adhesions between the two organs may, to some extent, account for the puzzling fact that in some cases of cholecystitis the pain is referred to the position of the vermiform appendix. Adenot ‡ has discussed the differential diagnosis of these two conditions in considerable detail. It is much less often that the converse mistake is made, and a case of appendicitis regarded as cholecystitis. But when the vermiform appendix is abnormally situated and runs up so as to come into close contact with the right lobe of the liver or even the gall-bladder, appendicitis may imitate cholecystitis very closely, as the pain and swelling are in the hepatic and not in the right iliac region. It may be pointed out that in the absence of any localising signs or of a history of gall-stone, the pain of cholecystitis is followed by more severe constitutional symptoms, such as collapse, than is the case in appendicitis. It should also be remembered that acute inflammation of the appendix and of the gall-bladder may be present at the same time.

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* Dieulafoy: La Presse Médicale, June 17, 1903, p. 445.

† Lorrain: Bull. Soc. Anat. Paris, 1903, p. 527.

‡ Adenot: Lyon Médical, t. xcvi, p. 227, 1901.

Prognosis.—In the milder cases of acute cholecystitis, which, however, are just those which are likely to be overlooked, the prognosis is good and the inflammatory process tends to subside rapidly. There is, however, a strong probability that gall-stones will result from the acute attack, and that biliary colic may possibly occur subsequently. In the more severe attacks the danger to life from ulceration and perforation must be faced, and the prognosis is much the same as in acute suppurative cholecystitis.

Treatment.—The patients should be kept in bed on a nourishing and easily digestible diet, and local pain treated by hot fomentations or, if severe, by the application of leeches. If the pain is very severe, morphine hypodermically may be required; but it has the grave disadvantage of masking the symptoms and should, therefore, be given with reluctance. Sickness should be controlled by effervescing draughts, bismuth, dilute hydrocyanic acid, or by fractional, $\frac{1}{20}$-grain, hypodermic injections of morphine. In cases where the temperature is high and there are signs of constitutional disturbance and the area of local peritonitis is increasing, surgical interference will very probably be required. In cases of a milder type salicylate of soda should be given, so as to increase the flow of bile through the ducts and so prevent extension of inflammation from the gall-bladder to the ducts. Solis-Cohen[*] recommends succinate of soda, and Reichmann[†] methylene-blue ($\frac{1}{2}$–$1\frac{1}{2}$ grains) in capsules. A mild laxative should be given to keep the bowels open and to favour evacuation of the inflammatory contents of the gall-bladder.

Sequelæ of Acute Cholecystitis.—Some cases of *serous distension* (hydrops) of the gall-bladder may be due to transient infective cholecystitis of very slight severity, in which there is a calculus at the neck of the gall-bladder preventing the exit of the inflammatory exudation through the cystic duct. (Kehr.[‡])

Chronic or Simple Empyema of the Gall-bladder.—Acute cholecystitis may develop into suppurative cholecystitis rapidly, so that the process is, for all practical purposes, suppurative inflammation of the gall-bladder throughout, or the symptoms of acute inflammation may pass off and be followed by a chronic infective condition of the gall-bladder which leads to the formation of pus inside the gall-bladder—simple or chronic empyema of the gall-bladder, as it has been called.

From the presence of pus in the gall-bladder these cases might be regarded as suppurative cholecystitis, but their clinical course is much ture usually remains normal. But if the inflammation is severe or extends to the ducts or to the peritoneal coat of the gall-bladder, there may be fever, sometimes of such a degree as to suggest suppuration, which, however, as shown by operation, is not present.

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[*] S. Solis-Cohen: Proc. Philadelphia County Med. Soc., vol. xxiii, p. 36.

[†] La Sem. Med., 1903, p. 140.

[‡] Kehr: Diagnosis of Gall-stones, p. 32, American translation.

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From the presence of gall-bladder these cases might be but their clinical course is much

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ounty Med. Soc., vol. xxiii, p. 30.

, American translation.

more like hydrops or dropsy of the gall-bladder. They bear the same relation to acute suppurative cholecystitis that a chronic abscess does to an acute one. In these cases there should be a history of acute cholecystitis in the past. Later there are abdominal pain, a tumor, and absence of fever. Cases of simple empyema of the gall-bladder may intermit, the swelling passing away and then recurring. In the following case cholecystitis supervened in early primary carcinoma of the gall-bladder and was followed by a chronic empyema:

T. G., fifty-six, a valet admitted Nov. 17, 1900, under my care, with jaundice and abdominal pain radiating to both shoulders, had been well until two months ago, when his appetite began to fail and vomiting came on. He then experienced sharp cutting pain, followed by vomiting. The pain recurred daily since. Jaundice was first noticed three weeks before admission. He has lost weight; motions are clay coloured.

There was a tense, tender tumor in region of gall-bladder, but no enlargement of the liver. Rectum normal. Free HCl in vomit. Jaundice became more marked. Much bile in urine; motions clay coloured. As pain continued and as it was desirable to prevent cholæmia, the probable diagnosis being carcinoma of the head of the pancreas compressing the common duct, Mr. Sheild operated, with a view of doing cholecystenterostomy on December 1, 1900: the gall-bladder was found to contain 6 ounces of offensive pus; there was a white growth on the surface near the middle, and a hard growth on its neck, as well as a mass near the pancreas. After evacuation of the gall-bladder a cholecystenterostomy (transverse colon) by means of Murphy's button was done. Next day the man was less jaundiced and bile came away freely from the wound. It is noticeable in connexion with the existence of empyema of the gall-bladder that during the patient's first fortnight in the hospital the temperature never went above 99°. He sunk in two days' time after the operation, apparently from asthenia.

At the autopsy there was extensive hæmorrhage around the gall-bladder, and the communication between that viscus and the colon leaked. The gall-bladder contained two small calculi, one in the neck, but not impacted. The growth seen during the operation was found microscopically to be a carcinoma invading the muscular walls of the gall-bladder. It was a columnar-celled growth undergoing transition to a spheroidal-celled type. The cystic, hepatic, and common bile-ducts were moderately dilated. There was a hard mass close to the head of the pancreas, adherent to the common bile-duct, and probably obstructing it. On section this mass, which was about the size of a pigeon's egg, was firm, white, and mottled with hæmorrhages. Microscopically it was a carcinoma showing a transition from a columnar- to a spheroidal-celled type. In this case cholecystitis supervened in early primary carcinoma of the gall-bladder, and was followed by a chronic empyema.

Ulceration of the gall-bladder may occur as the result of acute cholecystitis without there being any suppuration. Acute cholecystitis also may pass into a condition of *chronic cholecystitis*, which may take one of two forms: (1) The atrophic sclerogenous, with great thickening of the walls of the gall-bladder, which ultimately contracts and becomes thick-walled and shrivelled up (*vide* p. 615). (2) The catarrhal form, in which there is a distended gall-bladder containing thick, ropy, mucous fluid. Calculi are very prone to be produced by this process.

Another result of acute inflammation of the gall-bladder is that although resolution takes place, adhesions form around the gall-bladder and connect it to the colon, pylorus, or duodenum. These adhesions may interfere with the functional activity of the stomach and give rise to "adhesion dyspepsia," pyloric stenosis, and dilatation of the stomach. These results are described under the morbid results of cholelithiasis (p. 736).

An attack of acute cholecystitis may occur and pass away, to be subsequently succeded by a series of relapses or by a more severe form of inflammation of the gall-bladder.

MEMBRANOUS CHOLECYSTITIS.

Synonyms: Croupous Cholecystitis; Fibrinous Cholecystitis.

Inflammation of the gall-bladder may give rise to the formation of a cast of its cavity, which to the naked eye, at any rate, exactly resembles the casts of the bowel in mucous colic (mucous colitis, membranous colitis). As long ago as 1818 Dr. Richard Powell * read a paper before the Royal College of Physicians of London (published two years later in the last volume of the Medical Transactions of the College) in which he described attacks of colic followed by jaundice in patients whose fæces contained membranes, but no calculi. In some of his cases mucous colic must have been present since "the membrane was passed in perfect tubes, some of them full half a yard in length and certainly sufficient in quantity to have lined the whole intestinal canal," but it is possible that a similar condition was present in the bile-ducts and gall-bladder.

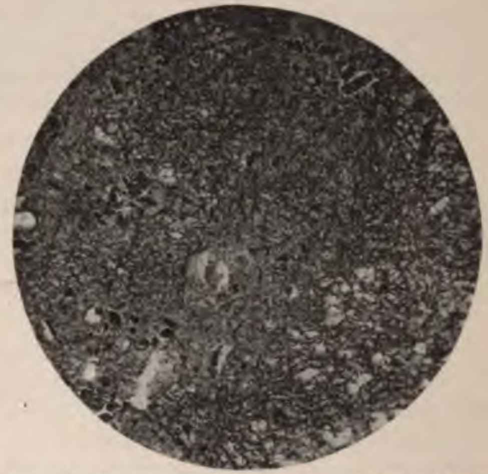

FIG. 74.—PHOTOMICROGRAPH SHOWING FIBRINOUS NETWORK ENCLOSING MASSES OF BLACK BILE-PIGMENT. (By S. G. Penny, Esq.)

Cases of gall-stone colic accompanied by membranes in the stools have been described by Mayo Robson and Macrae,† and by P. C. Fenwick.‡ In one of Mayo Robson's cases 78 calculi were afterwards removed from the gall-bladder, and in Fenwick's case the patient had almost certainly passed gall-stones previously. In a woman whose gall-bladder Mr. Allingham opened at St. George's Hospital a fibrinous cast of the gall-bladder surrounding a single large calculus was found and removed.§ In a case of membranous cholecystitis operated upon by Moynihan ‖ 368 calculi were removed. It is, therefore, probable that membranous cholecystitis is usually associated with calculi in the gall-bladder.

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* Powell, R.: Medical Trans. College of Physicians, vol. vi, p. 106, 1820.

† Robson and Macrae: Diseases of the Gall-bladder and Bile-ducts, p. 32, 2d ed., 1900.

‡ Fenwick, P. C.: Brit. Med. Journ., 1898, vol. i, p. 1072.

§ *Vide* Trans. Path. Soc., vol. liii, p. 405.

‖ Moynihan: Brit. Med. Journ., 1903, vol. i, p. 187.

Microscopically in the case I examined there was a fibrinous network enclosing bile-pigment and hexagonal crystals. In the outer layers of the cast there were round-cells, but no trace of the mucous membrane of the gall-bladder was found. The fibrinous structure differs entirely from the microscopic appearances of the casts of the intestine passed in mucous colic.

Clinically the symptoms are those of gall-stone colic, from which it can be distinguished only by finding membranous casts instead of calculi in the motions. The condition may be found only when the gall-bladder is open in the course of an operation, as in the following case:

A woman aged fifty-two who had never had jaundice or biliary colic was seized with pain in the right side of the abdomen and vomiting on Nov. 14, 1900. On admission two weeks later a tumor of stony hardness was found in the right iliac fossa, separated by a zone of resonance from the liver dulness. It was thought to be probably carcinoma of the colon. Laparotomy was performed by Mr. Allingham, and revealed a greatly enlarged gall-bladder with adhesions to adjacent parts. It was opened, and a single gall-stone, rather bigger than a walnut, was found enclosed in a thick fibrinous sac about ¼ inch thick. The calculus and the cast were removed, but the gall-bladder was left. This envelope was quite distinct and easily separable from the lining of the gall-bladder. Microscopic sections of the walls of the membranous sac showed a fibrinous network enclosing bile-pigment and hexagonal and quadrilateral crystals. The patient made a good recovery.

The *treatment* of an attack is the same as that of gall-stone colic, but if attacks recur, the gall-bladder should be opened and calculi removed. Moynihan* considers that the gall-bladder should be removed, but it appears to me doubtful whether there are as yet sufficient grounds for this dictum.

SUPPURATIVE CHOLECYSTITIS.

In this condition inflammation of the walls of the gall-bladder gives rise to an accumulation of pus in its cavity and may go on to ulceration and perforation. There are two conditions which have in common the production of pus inside the gall-bladder, but differ in their clinical course and aspects. In one—chronic empyema of the gall-bladder—pus is slowly formed within the gall-bladder, and its features are much the same as those of distension of the gall-bladder with mucous fluid (dropsy of the gall-bladder). In the other there is an acute suppurative inflammation. Except where specially stated, the following description refers to the latter condition. Chronic empyema is referred to on page 601. It is difficult to draw a hard-and-fast line between the less severe cases of acute suppurative cholecystitis and chronic empyema of the gall-bladder. Acute suppurative cholecystitis, when very acute, is described as phlegmonous cholecystitis.

The causes of suppurative cholecystitis are much the same as those of cholecystitis in general, and need not be repeated in detail. Acute suppurative cholecystitis is frequently associated with the presence of gall-stones.

Thus in 55 cases of suppurative cholecystitis collected by Courvoisier 41 were associated with cholelithiasis.

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* Moynihan: Brit. Med. Journ., 1903, vol. i, p. 186.

Impaction of a calculus in the cystic duct or neck of the gall-bladder favours microbic infection, as any micro-organisms reaching the gall-bladder by the blood-stream are retained and able to multiply. It is possible that in some cases of suppurative cholecystitis a calculus may have been previously expelled, but the presence of gall-stones is no more necessary than are enteroliths in appendicitis. Obstruction of the cystic or common bile-duct may act in a similar manner. Primary carcinoma of the bile-ducts may thus become complicated by suppurative cholecystitis, as shown in the following complicated case:

Carcinoma of Cystic Duct; Round Worm in Common Bile-duct; Suppurative Cholecystitis.—A woman aged forty-three, after long-continued and vague pains suggesting biliary colic, became intensely jaundiced, developed a high temperature, and died. There were gall-stones in the gall-bladder and suppurative cholecystitis due to a member of the colon group, primary carcinoma completely obstructing the cystic duct, and a dead lumbricoid worm in the common bile-duct which, it was thought, had conveyed the infection. (Etienne.*)

Suppuration may spread into the gall-bladder from suppurative cholangitis due to various causes, such as the rupture of a hydatid cyst into the ducts. In typhoid fever suppurative cholecystitis may occur, but it is fortunately rare, and is not so often seen as catarrhal cholecystitis.

In 494 cases of typhoid fever observed during six years at Montreal there were 25 deaths, among which there was one due to suppurative cholecystitis.† There were also 3 cases of acute cholecystitis that recovered. In 2000 fatal cases at Munich tabulated by Hölscher there was 5 of cholecystitis with suppuration.‡ In 1016 cases of typhoid fever treated during the two years 1900–1901 in the Imperial Yeomanry Hospitals in South Africa there was one case of suppurative cholecystitis.

Morbid Anatomy.—The gall-bladder is usually enlarged, sometimes very considerably, but in cases where suppuration occurs in a gall-bladder shrivelled up and contracted from recurrent attacks of cholecystitis there is no enlargement. The peritoneal coat is inflamed, granular from adherent lymph, and usually darkish red or greenish black in colour. It may be adherent by old fibrous adhesions to the parts around, or glued to them by recent lymph. Inflammation may thus spread to adjacent coils of intestine and cause paralytic distension. The wall of the gall-bladder is swollen from inflammatory exudation and softened and friable. The mucous membrane is largely replaced by granulation tissue, and the inner surface is shaggy, red, and in places has flakes of adherent lymph. Ulceration is commoner near the fundus, from the fact that calculi are more likely to gravitate there. The contents are bile-stained or sanious pus, and calculi are often present.

In cases of chronic empyema the walls of the gall-bladder are thickened from organisation of the inflammatory exudation.

Clinical Picture.—The signs and symptoms of acute cholecystitis vary considerably. They may be local, and at first confined to the region of the gall-bladder, or general, from wide-spread infection of the peritoneum.

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* Etienne: Archiv. général. de Méd., 1896, tome clxxviii, p. 284.

† Gillies: Montreal Med. Journ., June, 1900, p. 422.

‡ Hölscher: Münch. med. Woch., 1891.

The local manifestations are those of inflammation in the situation of the gall-bladder, pain, tenderness, and increased resistance of the overlying rectus abdomin is muscle.

The gall-bladder may be palpable as a tense tumor, somewhat pear-shaped, in a line between the tip of the ninth rib and a point one inch below the umbilicus in the middle line (Mayo Robson). The shape of the gall-bladder is subject to considerable variation: when elongated, it may appear to be independent of the liver, since it may be separated from the liver dulness by a zone of resonant intestines. When suppuration occurs in a gall-bladder which has previously been considerably distended, the tumor may be palpable in the right iliac fossa and may suggest appendicitis. In such cases there is often an elongated condition of the right lobe of the liver (Riedel's lobe). In exceptional instances the gall-bladder is found in the middle line of the abdomen.

When there is local peritonitis around the gall-bladder, intestinal paralysis and distension may prevent its being felt, but the hypochondrium will be prominent and exquisitely tender. In other cases rigidity of the abdominal muscles prevents the gall-bladder from being made out, unless the examination is conducted under an anæsthetic.

In many instances the gall-bladder is contracted from past attacks of inflammation, and though acutely inflamed and containing pus, does not project beyond the margin of the right lobe.

Pain is constant, as a rule, but exacerbations of great severity resembling biliary colic may occur, and its intensity is subject to considerable variation in different cases. It is usually felt in the right hypochondrium or pit of the stomach, but may be referred to the right iliac region and imitate appendicitis. In acute suppurative cholecystitis the temperature is raised and may be high, and be accompanied by rigors and attacks of shivering.

When pus has slowly formed—chronic empyema—in the gall-bladder there may be no rise of temperature and very little constitutional disturbance, though pain, loss of appetite, malaise, and some degree of wasting are usually present. If there is ulceration of the gall-bladder, septic absorption may give rise to fever, and local peritonitis with increased pain will result.

The pulse is rapid—100–120—in suppurative cholecystitis. An increasing pulse-rate shows that operative interference is indicated. There may be vomiting, from the irritation of the peritoneum around the gall-bladder, while the local peritonitis thus produced may spread to neighbouring coils of the small intestines or to the hepatic flexure of the colon and lead to paralysis of the bowel and so to the symptoms of intestinal obstruction. Jaundice is not a necessary symptom, and is very commonly absent. When present, it is usually slight. It may be due to extension of inflammation into the common bile or hepatic ducts, or to definite causes of biliary obstruction, such as gall-stones or tumors involving the large extra-hepatic bile-ducts. It has been suggested that when the mucous membrane of the gall-bladder is ulcerated, bile may be absorbed from the gall-bladder and that slight icterus in the early stages of suppurative cholecystitis, before the cavity becomes filled with pus, may be due to this cause, but this is unlikely.

The spleen is occasionally found to be enlarged. Albuminuria may be present in the more severe cases, and is due to the local action on the renal epithelium of poisons absorbed from the gall-bladder. There is leucocytosis of from 15,000 to 30,000. In severe cases there may be nothing to indicate that the primary lesion is in the gall-bladder, the symptoms being those of general peritonitis or intestinal obstruction, and thus imitating those due to perforation of the intestine or appendix.

If operation is delayed, the localising symptoms present in an early stage become masked by the spread of the inflammation to the general cavity of the peritoneum.

Complications and Results.—The chief danger of suppurative cholecystitis is perforation into the general cavity of the peritoneum and fatal peritonitis.

Keen * has collected 31 examples of perforation due to typhoidal cholecystitis; of these, 26 were not operated upon and all proved fatal; 5 were operated upon, and of these, 3 recovered.

Perforation of the gall-bladder may lead to a local peritoneal abscess instead of to general peritonitis. The formation of a local abscess is favoured by the presence of previous peritoneal adhesions shutting off the cavity of the general peritoneum. The abscess may open in a number of various situations, and imitate other forms of local abdominal suppuration, such as a subdiaphragmatic abscess due to disease of the stomach, duodenum, pancreas, etc. The abscess may discharge into the stomach, duodenum, colon, or penetrate the diaphragm and set up an empyema or a bronchobiliary fistula; or it may open through the skin of the anterior abdominal wall close to the costal arch or at the umbilicus. In rare instances the abscess may communicate with the pelvis of the right kidney, or even the bladder or vagina.

A suppurating gall-bladder may ulcerate directly into the liver and give rise to an abscess continuous with the cavity of the gall-bladder.

Weir † records the case of a woman aged thirty-five whose gall-bladder contained 3 ounces of pus. Ulceration on the posterior wall of the gall-bladder led into an abscess cavity in the liver containing more than an ounce of pus. A woman aged fifty-three died in St. George's Hospital with multiple recurrent growths after removal of the mamma; the cystic duct was blocked by a calculus; the gall-bladder contained pus and communicated by two openings with a small abscess cavity in the liver.

Concomitant suppurative cholangitis may lead to multiple areas of suppuration in the liver; these readily infect the hepatic veins, induce secondary abscesses in the lungs, which in their turn may burst into the pleura and set up empyema. A very rare event is profuse hæmorrhage into the gall-bladder from ulceration of the vessels; concomitant jaundice probably increases the tendency to hæmorrhage.

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* Keen: Complications and Sequels of Typhoid Fever, 1898, pp. 249, 325.

† Weir: Medical Record (U. S. A.), 1900, p. 1137.

Appendicitis may complicate suppurative cholecystitis, and in operating on a case of cholecystitis the condition of the appendix should be investigated, as death may subsequently occur from peritonitis due to perforation of the appendix in a case where suppurative cholecystitis has been satisfactorily operated upon. Dieulafoy * considers that the infection of the appendix is secondary to that of the gall-bladder.

Diagnosis.—Before perforation has occurred suppurative cholecystitis resembles other forms of local peritonitis in the neighbourhood, such as might be set up by a duodenal ulcer before perforation, by a localised subphrenic pneumothorax on the right side, due to a perforated duodenal or gastric ulcer, or to appendicitis in an abnormally situated appendix.

In addition to the signs of local peritonitis the presence of a tumor moving with respiration in or near the situation of the gall-bladder is an important indication of cholecystitis. The absence of jaundice must not be regarded as militating against the existence of cholecystitis, though the history of past attacks of biliary colic with transient jaundice strengthens the diagnosis.

Differential Diagnosis.—As already indicated, suppurative cholecystitis must be diagnosed from local peritonitis and subphrenic abscess due to other causes, but situated in the neighbourhood of the gall-bladder. It must also be distinguished from appendicitis and biliary colic.

In duodenal ulcer there should be a history of pain about two hours after food, but, unfortunately, the ulcer may remain latent until it perforates and sets up general or localised peritonitis. In most cases of duodenal ulcer there is no special resemblance to suppurative cholecystitis; but in the following case a perforating duodenal ulcer imitated acute influenzal cholecystitis:

A man about forty years of age had had recurrent attacks of influenza, but was improving until he was seized with vomiting and severe pain over the region of the gall-bladder. There was a rather indefinite history of biliary colic some years before. The patient had been slightly yellow during his illness, but showed no jaundice at the time that I saw him in consultation with Dr. Norman McCaskie. The man looked ill, had a temperature of 103°, and a rapid pulse. There was tenderness over the gall-bladder, but nothing like a tumor could be felt. Influenzal cholecystitis was diagnosed. Three leeches were put over the tender area. After this he was better until the next day, at 1 P. M., when he was suddenly seized with intense pain and collapse. I saw him again with Dr. McCaskie, and felt sure that perforation had taken place. Accordingly, Sir W. H. Bennett saw him and opened the abdomen and found that there was a perforated duodenal ulcer and not cholecystitis. The patient died two days after the operation.

Perforation of a gastric ulcer with the production of a localised subphrenic abscess hardly ever imitates suppurative cholecystitis, as the abscess nearly always contains air (a subphrenic pyopneumothorax), but in the following case the absence of resonance led to an open diagnosis:

A woman aged twenty-eight years had sudden pain on November 14, 1900. She came up to St. George's Hospital on November 16th with a firm mass, tender and dull on percussion, in the position of the gall-bladder. She had no jaundice, and there was no history of gall-stone colic, but she had previously had some dyspeptic pain one hour after food. The pulse was 140, and the patient's face indicated grave abdominal mischief. The diagnosis lay between suppurative cholecystitis and a local abscess due to a perforated gastric ulcer. My colleague, Mr. Sheild, operated the same day and found a localised peritoneal abscess due to perforation of a gastric ulcer close to the pylorus. The localised condition was due to old adhesions.

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* Dieulafoy: La Presse Médicale, June 17, 1903, p. 448.

An elongated and distended gall-bladder may project into the right lower half of the abdomen and simulate appendicitis; as already mentioned, this condition is frequently associated with an elongated right lobe of the liver. Cases of cholecystitis are not infrequently regarded as appendicitis; the converse mistake is much rarer. The differential diagnosis is very difficult, as both these conditions may vary so much in their clinical manifestations. Further, as pointed out above, cholecystitis and appendicitis may both be present at the same time. It is, therefore, desirable that during laparotomy for either of these conditions the state of the other viscus should, if possible, be investigated.

When perforation of a suppurating gall-bladder sets up general peritonitis, the diagnosis must be made from other forms of peritonitis, especially that set up by fulminating appendicitis, which it often closely resembles inasmuch as the pain may be referred to the right iliac fossa, probably because the contents of the gall-bladder may travel down into the region of the appendix. A careful investigation of the history may be of help in forming an opinion, but in either case immediate operation is essential and the surgeon must be prepared for unexpected conditions. When the abdomen is opened the character of the exudate may assist the surgeon by indicating the perforated viscus; thus bile or calculi will at once direct his attention to the gall-bladder; an acid reaction or gas, to perforation of the stomach or duodenum.

Prognosis.—In acute suppurative inflammation of the gall-bladder there is little tendency to spontaneous cure by the discharge of the purulent contents through the cystic duct, and subsidence of the inflammatory process, since in most cases the cystic duct is blocked or obstructed. This may be due to various factors, such as an impacted calculus, the contraction of cicatricial fibrous tissue, either as the result of past ulceration or from pericholecystic adhesions, or in some cases to new-growth involving the duct. When the obstruction of the cystic duct depends on swelling of the mucous membrane, due to the spread of inflammation from the gall-bladder, it is possible that the purulent contents may be expelled through the duct. In cases where the progress is less acute, pus may be formed in the gall-bladder and may remain confined there; this is chronic empyema of the gall-bladder. But in acute suppurative cholecystitis the inflammatory process spreads through the walls of the gall-bladder, infects the surrounding peritoneum, and leads to local or general peritonitis. Under the circumstances, therefore, the prognosis is grave unless operative interference is invoked before more widespread infection has set in. A local abscess may be treated surgically very successfully, but if general peritonitis has supervened, the outlook is very gloomy indeed.

Treatment.—The proper treatment of suppurative cholecystitis and of the more chronic condition, empyema of the gall-bladder, is surgical and consists in opening the gall-bladder and draining it, or, if it appear necessary, removing it. Exploratory puncture through the abdominal walls with a syringe to see whether there is pus is dangerous, and should never be countenanced. The palliative or medical treatment is the same as in acute cholecystitis.

PHLEGMONOUS CHOLECYSTITIS.

This is a very acute infective form of cholecystitis, and differs only in degree from the acute suppurative form just described, from which it cannot be separated by any hard-and-fast line. It passes into gangrenous cholecystitis, from which again it can hardly be separated; in fact, gangrene is merely a result of phlegmonous cholecystitis.

It may supervene on the same conditions as suppurative cholecystitis, such as cholelithiasis, typhoidal cholecystitis (v. Wunscheim,* Imhofer), and is due to a very virulent infection.

Incidence.—Very few cases are on record. Osler considers it much less rare than it is thought to be. Probably many cases described as acute suppurative cholecystitis might be included under this heading. Courvoisier, who first described it as acute progressive empyema of the gall-bladder, collected 7 cases, Mayo Robson † has added 4 more.

Morbid Anatomy.—The changes are the same as in acute suppurative cholecystitis, but more extensive and acute. The outside of the gall-bladder is purple, œdematous, and inflamed with adherent lymph. The walls are swollen, friable, and infiltrated with pus and blood; the mucous membrane is swollen, and may show ulceration, necrosis, or be separated in flakes from the underlying coats. The gall-bladder contains pus and often gall-stones. The cystic duct is closed and may be blocked by a calculus.

Clinical Features.—Symptoms set in suddenly with pain in the region of the gall-bladder. Owing to the intensity of the inflammation the peritoneum early becomes involved, at first locally, but soon peritonitis becomes generalised, unless there are firm adhesions around the gall-bladder.

Jaundice may be present from concomitant inflammation of the ducts, but it is inconstant, and therefore not of any great diagnostic value. The results are peritonitis, ulceration, sloughing, and perforation of the gall-bladder, leading to localised or generalised peritonitis, and a very rare event—gangrene of the gall-bladder.

The diagnosis depends on evidence of acute inflammation in the region of the gall-bladder in a patient whose history points to past cholecystitis. In some cases there may only be evidence of general peritonitis with or without the history that it followed localised inflammation in the right upper quadrant of the abdomen. When there is more or less localised inflammation of the peritoneum in the right upper half of the abdomen, the differential diagnosis is the same as in other forms of cholecystitis, to which the reader should refer. It may be very difficult when general peritonitis is established to make out whether it is due to fulminating appendicitis or to cholecystitis. Perforation of a gastric or duodenal ulcer may be suspected from the history, and receives very considerable support from signs, such as absence of the liver dulness, which points to the presence of free gas in the general peritoneal cavity. But the accurate diagnosis of phlegmonous cholecystitis is extremely difficult; this is shown by the following case, in which the gall-bladder showed a transition from phlegmonous to gangrenous cholecystitis.

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* v. Wunscheim: Prag. med. Wochen., 1898.

† Robson and Macrae: Diseases of the Gall-bladder. Robson: Brit. Med. Journ., 1903, vol. i, p. 189.

A woman aged sixty-three was admitted into St. George's Hospital with a history of constipation for three days and of more acute symptoms and vomiting for twenty-four hours. The sac of an umbilical hernia which she had had for three years was opened, and was found to contain adherent omentum, coils of small intestine, and a piece of the colon. The bowel, which was in good condition and was not strangulated, was returned. She temporarily rallied, but died with recurrent vomiting thirty hours after the operation. At the post-mortem there was general peritonitis. The gall-bladder was adherent to the colon, and contained several gall-stones in the fundus; its mucous membrane was ulcerated and in a necrotic condition, especially on the anterior surface of the gall-bladder. There was a large calculus encysted in the neck of the gall-bladder which occluded the commencement of the cystic duct. (*Vide* Fig. 75.)

The **prognosis** is very grave, as the disease may prove fatal in a few days, the process being so virulent that infective peritonitis is rapidly set up. The process is too acute to allow adhesions capable of localising the infection to be formed.

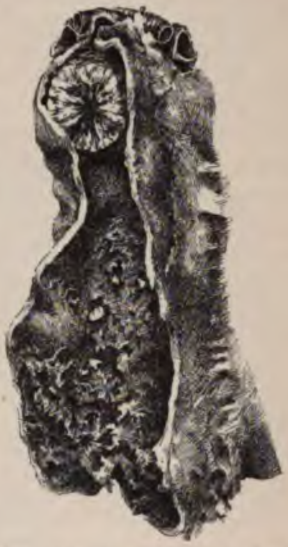

FIG. 75.—GALL-BLADDER WITH A LARGE CALCULUS IN ITS NECK AND SHOWING PHLEGMONOUS INFLAMMATION PASSING ON INTO GANGRENE. (Drawn by Dr. E. A. Wilson.)

The **treatment** is generally that of perforative peritonitis, and though the pain may be relieved by hot fomentations and the hypodermic injection of morphia, the only satisfactory measure is laparotomy and surgical treatment of the gall-bladder. The gall-bladder must either be freely drained, the surrounding space being packed with gauze—and this is probably the most satisfactory course—or the gall-bladder must be removed; this course is essential when the further stage of gangrene is threatened.

GANGRENOUS CHOLECYSTITIS.

Synonym: Gangrene of the Gall-bladder.

This is a further stage, or rather a result, of the very acute infective or phlegmonous inflammation of the gall-bladder just described, and, as already pointed out, no hard-and-fast line of distinction can be drawn between them. The transitional cases with small areas of necrosis in the gall-bladder may be spoken of as partial gangrene, as in Donoghue's [*] case. It stands in the same relation to cholecystitis that gangrenous appendicitis does to other forms of inflammation of the appendix, but it is very rare and thus contrasts with the frequency of gangrenous appendicitis. It seems probable that the rarity of gangrene of the gall-bladder may in part be explained by its better blood-supply and by the fact that it is not prone, like the appendix, to be twisted on its own axis and its blood-supply thus interfered with. In order that gangrene may supervene it is necessary that the cystic duct should be occluded and that a very virulent infection should fall on the gall-bladder. Gibbon [†] described a case in which impaction of a calculus at the neck of the gall-bladder probably interfered with the blood-supply; a similar condition is seen in figure 75, but it must be remembered that cholecystitis frequently supervenes in cases where a calculus is impacted in the neck of the gall-bladder without causing gangrene of the gall-bladder.

Incidence.—It is extremely rare, but probably not so rare as the recorded cases suggest. It is highly probable that some cases have been published or described merely as very severe cholecystitis. Cases have been reported by Hotchkiss,[‡] Mayo Robson,[§] Mayo,[‖] Gibbon,[**] Moynihan.[††]

The **morbid anatomy** is the same as in phlegmonous cholecystitis, with the addition of gangrene of the wall of the gall-bladder. The extent of the gall-bladder affected by gangrene varies, but it appears to begin at the fundus and spread towards the neck of the gall-bladder. The gangrenous walls are dark green in colour, extremely soft, and friable.

The cystic duct is blocked, and there may be a calculus imbedded in the neck of the gall-bladder. Calculi are present in the gall-bladder in Hotchkiss', Gibbon's, Moynihan's cases, and in a case described as phlegmonous cholecystitis by Da Costa,[‡‡] where the calculus was found projecting through a hole in the wall of the gall-bladder.

The **clinical features** are the same as those of "phlegmonous" cholecystitis in a late stage—viz., general peritonitis. In fact, as has already been pointed out, gangrenous cholecystitis is the extreme stage of the phlegmonous form. In Gibbon's case there was a leucocytosis of 37,600, which fell to 12,600 in twenty-four hours after removal of the gall-bladder.

The **diagnosis** is extremely difficult, and cannot be made from perforative peritonitis due to other lesions of the gall-bladder. It is very likely to be confused with peritonitis due to fulminating appendicitis.

The only real **treatment** is surgical, and consists in removal of the gall-bladder (cholecystectomy). There should be no delay in operating on any case which is thought to be one of phlegmonous or gangrenous cholecystitis.

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[*] Donoghue: Amer. Journ. Med. Sciences, vol. cxxiii, p. 193.

[†] Gibbon: Amer. Journ. Med. Sciences, vol. cxxv, April, 1903, p. 592.

[‡] Hotchkiss: Annals of Surgery, Feb., 1894.

[§] Mayo Robson: Brit. Med. Journ., 1903, vol. i, p. 181.

[‖] Mayo, quoted by Gibbon.

[**] Gibbon: Loc. cit.

[††] Moynihan: Brit. Med. Journ., 1903, vol. i, p. 186.

[‡‡] Da Costa: Proc. Philadelphia County Med. Soc., vol. xxiii, p. 29.

Mayo Robson * and Moynihan † have both operated successfully in cases of partial gangrene of the gall-bladder.

In addition to surgical treatment, morphine should be given and the patient's strength maintained by strychnine and nutrient enemata.

CHRONIC CATARRHAL CHOLECYSTITIS.

This is a chronic inflammatory condition in which, as in catarrhal appendicitis, subacute attacks supervene from time to time and produce pain resembling that of biliary colic.

Causes.—It may be a legacy left by a past attack of acute inflammation of the gall-bladder, and is often associated with gall-stones. In other cases the process is probably chronic from the first, and may be disposed to by sedentary habits, constipation, tight lacing, and the other factors that favour the microbic infection of the gall-bladder. Chronic catarrhal cholecystitis may be part of a chronic catarrhal state of the ducts, and is then quite subordinate to that condition.

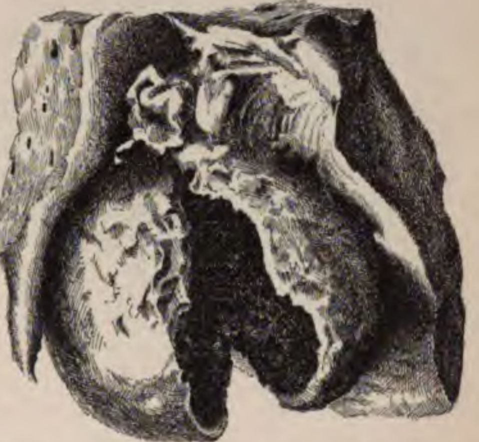

FIG. 76.—DRAWING OF CALCAREOUS INFILTRATION OF THE GALL-BLADDER.

From a specimen (Series ix, No. 195 A) in the Museum of St. George's Hospital. (Drawn by Dr. E. A. Wilson.)

Morbid Anatomy.—The gall-bladder is usually somewhat distended with mucus, which may be so thick and tenacious as to resemble grains of boiled sago (Mayo Robson ‡). It may or may not contain calculi; occasionally calculi are embedded in the walls of the gall-bladder (parietal calculi). According to Mayo Robson, adhesions between the gall-bladder and adjacent organs are found when the gall-bladder contains calculi, but not otherwise. The walls of the gall-bladder are thickened, and the rugous appearance of the mucous membrane may be exaggerated, but in some instances the mucosa, though thickened, is smooth and has a white, nacreous appearance. From contraction of inflammatory tissue the gall-bladder may become small and shrivelled up (cholecystitis obliterans). Secondary calcification of the walls sometimes occurs. The cystic duct is often quite pervious.

Microscopically the thickening of the wall of the gall-bladder is due to fibrosis and proliferation of connective tissue between the muscular and serous coats. There may be a large amount of well-formed connective tissue with a little intervening small-cell infiltration due to proliferation of the connective tissue. There may also be some œdema and swelling, and sometimes hyaline degeneration of the well-formed fibrous tissue. I have not observed the elongation of mucous glands through the muscular coat to the serosa described by Ries,* and am inclined to consider such a process as evidence of early malignant disease.

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* Mayo Robson: Brit. Med. Journ., 1903, vol. i, p. 181.

† Moynihan: Brit. Med. Journ., 1903, vol. i, p. 186.

‡ Mayo Robson and Macrae: Diseases of the Gall-bladder and Bile-ducts, p. 31.

Clinically, the symptoms are practically those of cholelithiasis. There are attacks of gall-stone colic from time to time. In the intervals, when the subacute attack of inflammation has subsided, there is no jaundice and no tenderness over the gall-bladder, which can sometimes be felt as a pear-shaped tumor. The distinction between chronic cholelithiasis with periodic attacks of colic and chronic catarrhal cholecystitis is an artificial one. From an academic point of view a criterion might be made of the presence or absence of gall-stones; the cases of chronic catarrhal cholecystitis associated with gall-stones might then be removed to another category and included under cholelithiasis. It is doubtful whether a diagnosis between chronic catarrhal cholecystitis and gall-stones can be made on the ground that the biliary colic is more severe in the case of gall-stones, since, after repeated attacks of biliary colic, the ducts may be so dilated that pain is comparatively slight. When there are no gall-stones, the attacks of colic due to attacks of subacute cholecystitis are less likely to be followed by jaundice, and no calculi can be recovered from the stools.

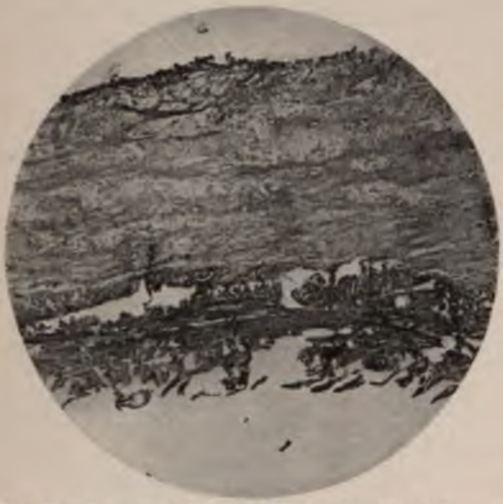

FIG. 77.—SECTION OF WALL OF GALL-BLADDER IN CHRONIC CHOLECYSTITIS.

The villosities of the inner coat are seen, but there is no epithelium left on the surface. The darker longitudinal strands are smooth muscle. The lighter portion, which constitutes two-thirds of the thickness of the wall, is fibrous tissue showing œdema and some small-cell infiltration. Low power. (Photomicrograph by Dr. H. Spitta.)

Treatment.—The medical treatment is that of cholelithiasis, viz., a careful dietary with plenty of water, salicylate of soda, regular action of the bowels, and exercise, and, if necessary, gentle massage. These measures are directed to prevent stagnation of bile in the gall-bladder and to increase the flow of bile through the ducts and gall-bladder so as to flush them.

Surgically drainage of the gall-bladder is followed by good results.

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* Ries: Annals of Surgery, Oct., 1902.

Excision of the gall-bladder, according to Ries,* is preferable to removing the mucous membrane of the gall-bladder and leaving the rest of the viscus, as practised by Mayo,† but in most cases drainage will probably be sufficient.

ATROPHIC SCLEROSING CHOLECYSTITIS.

Synonym: Cholecystitis obliterans.

This thickened, retracted condition of the gall-bladder is the result of chronic cholecystitis and is often associated with cholelithiasis of old standing. The gall-bladder is buried in adhesions and firmly contracted on itself, or perhaps on one or more calculi. In such cases the wall of the gall-bladder is often almost inseparable from the calculi. If the calculus is a large one, the gall-bladder may be palpable as a tumor of stony hardness.

The walls of the gall-bladder may undergo calcification, and cholesterin may be deposited in the tissues.

When extensively calcified, the gall-bladder may be felt through the abdominal wall and will resemble a gall-bladder filled up with a large gall-stone.

Claude ‡ found a calcified gall-bladder the size of a turkey's egg in a woman aged ninety-four

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* Ries: Annals of Surgery, Oct., 1902.

† Mayo: Annals of Surgery, 1899.

‡ H. Claude: Bull. Soc. Anat., 1897, p. 219.

PARASITIC AFFECTIONS OF THE GALL-BLADDER.

Hydatid cysts hardly ever arise in the gall-bladder itself. Cases have been reported in the last twenty years by Bowman,[*] J. K. Thornton,[†] F. Page,[‡] Langenbuch,[§] Huber,[‖] and Barling and Burton.[**] McGavin's[††] case was in a woman aged thirty-two years and was removed during life, but the committee of the Pathological Society, on which I was, reported that the cystic tumor was not the gall-bladder, but a hydatid cyst which had arisen in its neighbourhood and probably displaced it. A number of cases described from clinical evidence, viz., jaundice, a distended gall-bladder, and disappearance of these signs after the passage of hydatid membranes by the bowel, as hydatid disease of the gall-bladder, are open to the criticism that they may have been examples of rupture of a hydatid cyst into the bile-ducts, with subsequent obstruction of the common bile-duct. Cysts have been said to have been found loose in the gall-bladder. It is conceivable that small daughter cysts which have passed into the ducts from rupture of a cyst into the ducts might pass up a cystic duct which had previously been dilated by a gall-stone, but it would hardly be possible for them to work their way up a normal cystic duct on account of the valves of Heister. As shown by J. Hutchinson, Jr.'s, case, a hydatid cyst in the liver may, under conditions such as suppuration, discharge into the gall-bladder. So far as our knowledge goes, the symptoms of hydatids in the gall-bladder are much the same as those of rupture of a hydatid cyst into the bile-ducts.

Distomum Hepaticum.—Budd, in his book on Diseases of the Liver, mentions cases in which liver flukes have been found loose in the gall-bladder.

Actinomycosis.—Mayo Robson[‡‡] operated successfully on a case of this nature, which appears to be unique.

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[*] Bowman: Lancet, 1876, vol. i, p. 532.

[†] Thornton, J. K.: Lancet, 1891, vol. i, p. 763.

[‡] Page, F.: Lancet, 1898, vol. i, p. 995.

[§] Langenbuch: Deutsch. med. Wochens., Bd. xxvi, 1900.

[‖] Huber: Deutsch. Archiv f. klin. Med., Bd. xlviii, S. 432.

[**] Barling and Burton: Birmingham Med. Rev., vol. xlii, p. 234.

[††] McGavin: Lancet, 1902, vol. i, p. 504. Trans. Path. Soc., vol. liii, p. 351.

[‡‡] Diseases of the Gall-bladder and Bile-ducts, p. 173, ed. iii.

INNOCENT TUMORS OF THE GALL-BLADDER.

Innocent tumors are rare in the gall-bladder and are not nearly so often met with as malignant growths. Practically the only innocent tumor met with in the gall-bladder is a papilloma.

PAPILLOMA OF THE GALL-BLADDER.

A papilloma of the mucous membrane of the gall-bladder is rather a rare tumor—far rarer than carcinoma. Zenker [*] has suggested that papilloma is the early stage of carcinoma; this may be true for some cases of villous carcinomata of the gall-bladder, but from an examination of an extremely early case of carcinoma I am convinced it is not universally true. Also, if it were so, routine examination of the gall-bladder would have shown that papillomata are commoner than is the case.

A papilloma may be associated with the presence of gall-stones, and from analogy it would be natural to expect that the papilloma is secondary to the irritation of calculi; but there may be no calculi and nothing to suggest that there ever have been any. It is probable that some of the recorded cases of villous carcinoma of the gall-bladder are really large innocent papillomata.

Chappet [†] describes a large villous cancer in the gall-bladder attached to the mucosa by two very thin pedicles in a man aged seventy-nine years; there was a calculus in the common bile-duct.

The papilloma is a soft wavy mass which is extremely friable and breaks up on examination so easily that it may, when removed at an operation, suggest the material that would later form a gall-stone. When seen after death the tumor is deeply bile-stained. A papilloma of the gall-bladder may become detached from its base and be found quite loose in the gall-bladder. This was the state of affairs in a female patient of Dr. Des Vœux's whose gall-bladder was operated upon by Mr. Allingham, who removed a pure cholesterin gall-stone, together with a soft, red coloured mass of villous growth from it. Microscopically there is a delicate papillomatous growth covered with columnar or subcolumnar cells. In specimens removed during life from the gall-bladder it is impossible, from microscopic examination, to say whether it is a simple papilloma or the superficial part of a villous carcinoma.

The structure of the papilloma removed after death is difficult to make out in the microscopic sections I have seen, from the staining and degeneration due to soaking in the bile. V. Schueppel [‡] examined microscopic sections of a myxomatous papilloma from a gall-bladder which did not contain any bile.

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[*] Zenker: Deutsche Archiv f. klin. Med., Bd. xliv, S. 159.

[†] Chappet: Lyon Médical, vol. lxxvi, p. 146.

[‡] v. Schueppel: v. Ziemssen's Cyclopædia of Practical Medicine, vol. ix, p. 56.

If the papilloma becomes œdematous or undergoes mucoid degeneration, a succulent tumor (myxomatous papilloma) results. No clinical symptoms can be correlated with papilloma of the gall-bladder.

The two following examples of papilloma of the gall-bladder have come under my notice at St. George's Hospital:

A man aged forty-five died in St. George's with cardiac dilatation secondary to arteriosclerosis. The gall-bladder felt rather like a varicocele, and when opened contained a yellow, bile-stained, papillomatous mass growing from the anterior surface of the gall-bladder close to the fundus. The wall was not thickened or invaded. There were no calculi in the gall-bladder or bile-ducts, but the common duct was dilated, as if by the passage of calculi previously. In a man who died of pulmonary tuberculosis at the age of thirty-nine the gall-bladder contained a small bile-stained papilloma. There were no calculi in the gall-bladder or ducts, and no dilatation of the ducts. There had been no abdominal symptoms.

FIBROMA.

A submucous fibroma of the gall-bladder has been described.* A caution may be thrown out, however, not to regard the early stage of primary carcinoma of the gall-bladder as a fibroma. The naked-eye appearance of early carcinoma may very closely resemble a firm fibroma.

CYSTIC ADENOMA.

These tumors are extremely rare and are pathological curiosities. Such a growth might be derived from the mucous glands embedded in the wall of the gall-bladder.

Stanmore Bishop † removed a cystic tumor from the gall-bladder of a woman aged forty-two years who had had bilious attacks accompanied by transient jaundice. The tumor contained a number of cavities which did not communicate with each other; the cysts were lined by cylindrical epithelium. Terrier and Auvray ‡ quote a case of Wiedemann's which was probably of the same nature.

CYSTS.

Cysts in the mucous membrane of the gall-bladder containing cholesterin and of small size are occasionally met with. Terrier and Auvray refer to a case of Adler's in which a gall-bladder presented three such cysts. These cholesterin-containing cysts may develop into calculi embedded in the wall of the gall-bladder. Hydatid cysts are referred to on page 616.

Local œdema under the peritoneal coat of the gall-bladder is sometimes seen in cases of backward pressure, such as is induced by morbus cordis or chronic bronchitis and emphysema. To the naked eye it looks like a small cyst; microscopically it is seen that there is no true cavity, and only œdema of the tissues.

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* Albers, quoted in v. Ziemssen's Cyclopædia of Practical Medicine, vol. ix, p. 567, 1880.

† Stanmore Bishop: Lancet, 1901, vol. ii, p. 72.

‡ Terrier and Auvray: Chirurgie du foie, p. 253, 1901.

FATTY TUMORS.

Local subperitoneal masses of fat are in rare instances seen on the gall-bladder. I have observed this abnormality in otherwise perfectly healthy gall-bladders. As a result of cholecystitis it is conceivable that an appendix epiploica might become adherent to the gall-bladder and subsequently be detached from the colon.

PRIMARY MALIGNANT DISEASE OF THE GALL-BLADDER.

This is by no means a rare disease, and has attracted quite a fair share of attention. Frerichs[*] gave an excellent account of the disease in 1861, and in 1870 Villard[†] collected 17 cases; Musser,[‡] in 1889, 100 cases; Courvoisier,[§] 103; and in 1901 Fütterer,[‖] 268. These tables, of course, deal largely with the same individual cases. The bibliography attached to Siegert's,[**] Ames's,[††] and Fütterer's papers shows that the subject has no cause to complain of neglect. Though this disease has certainly received more attention of late years, it is probably actually more frequent now than formerly. Of Fütterer's 268 cases, no less than 195 were reported since 1880. This is no doubt in part due to the fact that the disease has been more generally distinguished from genuine primary carcinoma of the liver.

It is a striking fact that another annexa of the alimentary canal, the vermiform appendix, in which concretions are comparatively common, is very rarely attacked by primary malignant disease.[‡‡] They are both frequently inflamed, and are both very liable to irritation and infection, the appendix more especially. Why one should be comparatively immune to malignant disease is a difficult question. Possibly some basis of an explanation may be found in the fact that the appendix is an atrophying relic of part of the gut, while the gall-bladder belongs to the very extensively developed appendage—the hepatic diverticulum from the duodenum.

MORBID ANATOMY.

Primary malignant disease of the gall-bladder is practically always carcinoma. I have references to nine cases of primary sarcoma.

Musser,[§§] in his statistical analysis, mentions three cases of primary sarcoma; Griffon and Segall[‖‖] record a case of a spindle-celled sarcoma, primary in the gall-bladder, which contained two calculi, in a woman aged seventy-six. Czerny (angio-sarcoma), Reidel,[***] and Neviadomski[†††] have also met with primary sarcoma of the gall-bladder. Becker[‡‡‡] has described a primary endothelioma of the gall-bladder associated with two gall-stones which had almost perforated into the stomach near the pylorus. I have examined one case of primary spindle-celled sarcoma of the gall-bladder.

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[*] Frerichs: Diseases of the Liver, vol. ii, p. 479. Transl. New Sydenham Soc.

[†] Villard: Bull. Soc. Anat. Paris, vol. xliv, p. 217, at sitting August, 1869.

[‡] Musser, J. H.: Boston Med. and Surg. Journ., vol. cxxi, p. 525, 1889.

[§] Courvoisier: Pathologie und Chirurgie der Gallenwege, Leipzig, 1890.

[‖] Fütterer, G.: Ueber die Aetiologie des Carcinoms, 1901, Wiesbaden.

[**] Siegert: Virchow's Archiv, Bd. cxxxiii, S. 353.

[††] Ames, D.: Johns Hopkins Hospital Bulletin, vol. v, No. 41, 1894.

[‡‡] Within the last few years a number of cases of primary carcinoma of the vermiform appendix have been described, and in 1903 Moschowitz (Annals of Surgery, part 126, p. 891) collected 21 authentic cases.

[§§] Musser: Loc. cit.

[‖‖] Griffon and Segall: Bull. Anat. Soc. Paris, 1897, p. 586.

[***] Riedel: Erfahrungen über die Gallensteinkrankheiten, 1892.

[†††] Neviadomski: Meditzinskoe Obozrenie, Feb., 1900.

[‡‡‡] Becker, W.: Journ. American Med. Assoc., 1903, April 4, p. 903

A woman aged fifty-six had a large tumor to the right of the umbilicus which entirely replaced the gall-bladder; it contained a cavity lined by broken-down growth which opened into the transverse colon. The growth had tracked along the cystic and common bile-ducts and formed a projection at the biliary papilla. No gall-stones were found. There were secondary growths in the aortic lymphatic glands and in a gland in the right groin. There was no jaundice. Microscopically the growth was a spindle-celled sarcoma somewhat alveolar in arrangement. There were numerous blood-spaces in the growth. The case was under the care of Mr. [now Sir] W. Bennett in St. George's Hospital in 1891 and the autopsy was made by me.

The description of malignant disease of the gall-bladder is, therefore, practically that of carcinoma of the organ.

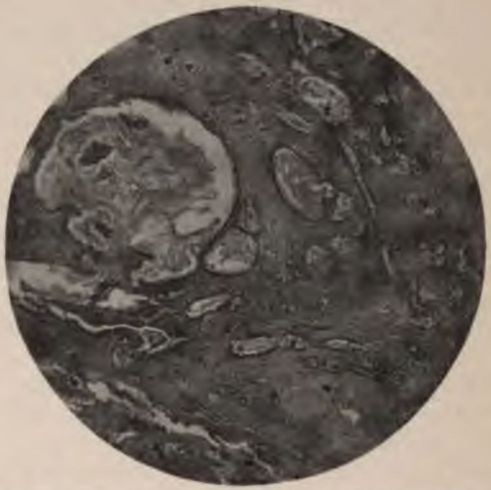

FIG. 78.—PHOTOMICROGRAPH OF COLUMNAR-CELLED CARCINOMA OF THE GALL-BLADDER.

Shows dilated spaces lined by columnar epithelium and containing mucus. (S. G. Penny, Esq.)

Histological Structure.—Carcinoma of the gall-bladder varies much, both in the form of the cells and in their structural arrangement; it may be either columnar or spheroidal-celled. The cells may undergo colloid degeneration, or the cavities of the tubes lined by columnar epithelium may become distended by mucoid material without the cells showing any of the appearances of colloid degeneration. The columnar-celled carcinoma may grow into the cavity of the gall-bladder as a villous or papillomatous growth; but the essentially malignant part, where there is invasion of the deeper layers, does not show a papillomatous arrangement, and is a columnar-celled carcinoma of the ordinary type, containing a fair amount of fibrous tissue. Frequently a change of type of the carcinoma is visible; parts of the growth may be columnar-celled, others cubical, and other parts spheroidal-celled. This transition is seen in columnar-celled carcinomata elsewhere, especially in duct cancer of the breast. In transitional parts, and especially when colloid or allied degenerative changes are present, the large epithelial cells may be so far modified as to appear flattened, and have then been described as squamous cells;* multinuclear cells are also sometimes seen. The lining membrane of the gall-bladder is normally columnar epithelium; as the result of inflammation or irritation it may become replaced by round cells, but metaplasia never goes so far as to lead to cornification. It is highly improbable that changes of this kind ever give rise to a true squamous-celled carcinoma, showing keratinisation, primary in the gall-bladder, though in transitional parts of the growth the altered or colloid columnar cells and cell inclusions may closely resemble squamous cells and cell-nests.

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* For a discussion of this curious change see Bret. Lyon Médical, t. lxxxix, p. 41, Sept. 11, 1898. Cases of this kind are recorded by Mayo Robson: Medico-Chirurg. Trans., vol. lxxix, p. 159; Hebb, R. G.: Westminster Hospital Reports, 1895, p. 316; Deetz: Virchow's Archiv, Bd. clxiv, S. 381.

Deetz (Virchow's Archiv, Bd. clxiv, S. 381), in an examination of 300 gall-bladders, including some with cholelithiasis, never observed transformation of the lining epithelium into squamous epithelium, but he nevertheless believes this change must occur to account for the appearances of a primary squamous-celled carcinoma of the gall-bladder. Adami (Brit. Med. Journ., 1901, vol. i, p. 626) also believes that metaplasia of the columnar into squamous epithelium must take place in the gall-bladder.

Degenerative changes besides the mucoid and colloid changes already referred to and fatty degeneration of the cells of the growth may occur, while in parts the growth may become necrotic. Occasionally hæmorrhages may take place into the tumor.

Starting-point of the Growth.—In order to explain the origin of the two varieties, columnar- and spheroidal-celled carcinoma, arising in the gall-bladder, it has been suggested that spheroidal-celled carcinoma is derived from the mucous glands in the wall of the gall-bladder, while columnar-celled carcinoma is derived from the surface mucous membrane of the gall-bladder. This theory is unnecessary, since the change in type from a columnar- to a spheroidal-celled carcinoma can be seen in the same specimen, and also because there is no essential difference between the columnar cells of the surface mucous membrane and of the mucous recesses, depressions, or "glands" in communication with it. It may be concluded that carcinoma, whatever its form, arises from the mucous membrane as a whole, and no statement that either form of carcinoma arises exclusively from the surface epithelium of the gall-bladder or from the epithelium lining the "glands" is necessary or justified by our knowledge.

It has been suggested that carcinoma of the gall-bladder begins as a papilloma,* which, like a polypus of the intestine, might be called an adenoma. Cases of pure papilloma of the gall-bladder are very rare. There are, moreover, some cases of carcinoma of the gall-bladder which do not show any villous projection into the lumen of the cavity, but are limited to the infiltration of the wall and the surrounding tissues. Although it may happen sometimes, there is certainly no proof that the growth always starts as an adenoma, which subsequently takes on malignant growth. Carcinoma of the gall-bladder may, like carcinoma of the intestine, occur in two forms: (1) That projecting into the cavity of the gall-bladder as a fungating growth; (2) that limited to an infiltration of its walls. The fungating form is generally papillomatous, and histologically a columnar-celled growth, while the infiltrating form, though it may be a columnar-celled carcinoma, is often a spheroidal-celled growth. The two forms may be combined.

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* Zenker: Deutsches Archiv f. klin. Med., Bd. xliv, S. 159, 1889; Aczel: Virchow's Archiv, Bd. cxliv, S. 86, 1896; Warthin: Journ. American Med. Association, May 6, 1899.

Situation of the Growth.—The fundus is the commonest situation for the origin of carcinoma, and the distal compartment of an hour-glass gall-bladder may be the starting-point of the growth. This is explained by the fact that the fundus being the most dependent part, is specially exposed to irritation from the presence of calculi. The growth may begin at the neck of the gall-bladder, at its junction with the cystic duct, and then give rise to obstruction, either by blocking the lumen or by spreading around the circumference of the narrowed gall-bladder or cystic duct, and producing an annular stricture. As a result the gall-bladder may become tense and distended with fluid. Carcinoma of the cystic duct is much the same as carcinoma of the neck of the gall-bladder, and clinically resembles that condition rather than carcinoma of the other bile-ducts. Carcinoma of the neck of the gall-bladder may appear to depend on the irritative effects of impacted calculi in that situation.

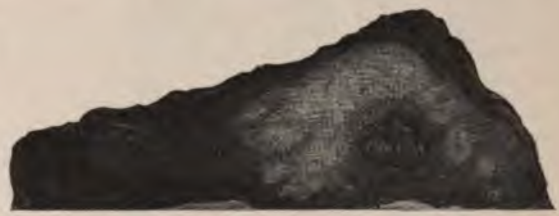

Fig. 79.—Drawing of Section of a White Growth Replacing the Gall-bladder, in the Centre of which there is a Calculous Mass.

From a specimen (Series ix, No. 197*c*) in St. George's Hospital Museum. (Drawn by Lawrence Jones, Esq., M.B., F.R.C.S.)

The growth may, however, involve the whole of the gall-bladder, so that it is difficult or impossible to say in what part—fundus, neck, etc.—it arose. In other cases the gall-bladder is entirely replaced by growth. That the growth originated in the gall-bladder is then assumed from the complete absence of that viscus, or from the presence of calculi embedded in the centre of a growth in the position of the gall-bladder. This condition may, indeed, be erroneously regarded as primary (massive form) cancer of the liver itself, the real origin of the growth in the gall-bladder, which has completely disappeared, being easily overlooked.

A secondary growth in the gall-bladder may, to the naked eye, resemble a primary neoplasm.

There is a specimen in St. Bartholomew's Hospital Museum (No. 2216 G) which looks like a primary growth, but is really, as shown by section of the walls of the gall-bladder, a secondary nodule of round-celled sarcoma; the primary growth was in the lung.

Behaviour and Appearance of the Growth.—The columnar-celled form may project into the gall-bladder and fill it with a villous or papillomatous growth which easily disintegrates, and then somewhat resembles caseous pus or plaster-like material, imitating both in structure and in appearance psorospermosis of the bile-ducts in a rabbit's liver. A columnar-celled carcinoma of the gall-bladder may form a hard, solid growth, and need not be in the least villous in its arrangement. So, just as in the breast, a columnar-celled carcinoma may occur in one of two forms: (i) villous; (ii) like an ordinary columnar-celled carcinoma of the bowel.

On comparing the columnar- and spheroidal-celled forms of gall-bladder carcinoma it is seen that, generally speaking, the spheroidal-celled grows more rapidly and generalises more freely. But a columnar-celled growth may spread by continuity into the liver substance, and then show a transition to the spheroidal-celled type.

Hæmorrhage from the villous growth into the gall-bladder very rarely occurs; Musser says that hæmorrhages occurred 7 times in 100 cases. It has seemed to me, as would naturally be expected, that colloid change occurs more commonly in the more chronic columnar-celled growths than in the spheroidal-celled carcinoma. Carcinoma, if seen in an early stage, may appear as a localised thickening, like a button, of the wall of the gall-bladder, of a whitish appearance, and may resemble a scar or a gumma. Opportunities for examining the early stage of such growths are rare; as a rule, the growth has extensively invaded the walls of the gall-bladder. (For an example of an early case *vide* p. 602.)

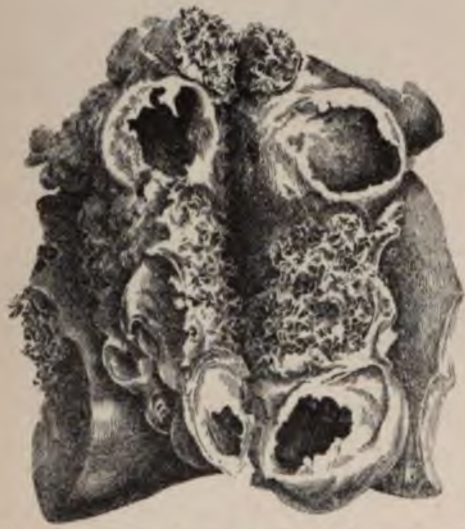

FIG. 80.—PRIMARY CARCINOMA OF THE GALL-BLADDER OF THE PAPILLOMATOUS FORM.

The gall-bladder has been cut up longitudinally; it is seen that the growth does not occupy the whole of the gall-bladder, the fundus and neck not being affected. From a specimen (Series ix. No. 197A) in St. George's Hospital Museum. (Drawn by Dr. E. A. Wilson.)

Extension of the Growth by Continuity.—As already mentioned, a large growth in the gall-bladder may directly invade the liver, and thus give rise to considerable hepatic enlargement. In these cases the fact that the growth arose in the gall-bladder may be overlooked and the condition may be regarded as primary carcinoma of the liver.

In one case which I examined the growth spread from the anterior surface of the gall-bladder into the liver substance, and projected so little into the cavity of the gall-bladder that it was only on section and careful examination that it became clear that the growth started in the walls of the gall-bladder. In this instance the primary growth was confined to the surface of the gall-bladder in contact with the liver, and might have been overlooked on casual examination, and the numerous secondary growths in the liver might, therefore, have been regarded as primary multiple carcinoma.

Generally, however, when the growth in the gall-bladder extends by continuity into the liver, the origin of the tumor is quite clear. The growth may spread by continuity in the wall of the cystic duct into the common bile-duct, or along the hepatic ducts into the liver, much in the same way that a growth at the bifurcation of the trachea may track along the bronchi and their lymphatics into the lung. It may then be difficult to say whether the primary growth started in the bile-ducts and then extended, or originated in the gall-bladder. A carcinoma of the gall-bladder has been known to project as a free process down the lumen of the cystic duct into the common bile-duct (Bohnstedt *), in the same manner that malignant disease of the liver has, in at least one case (Gilbert and Claude †), been found projecting into the extra-hepatic bile-ducts.

Fistulæ.—When, as is more commonly the case, the growth begins in the fundus of the gall-bladder, it readily becomes adherent to the colon and may open into it. Musser refers to this accident in 10 cases. Fistulous communications between the colon and gall-bladder may, of course, be due to other causes, such as ulceration due to a gall-stone, but in 9 cases of colocholecystic fistulæ collected by Murchison 6 were the result of cancer of the gall-bladder. In like manner the carcinomatous gall-bladder may open into the duodenum, but this fistulous communication is less often seen in carcinoma than in cholelithiasis.

The growth may involve the duodenum so widely that it may be difficult to decide in which situation it started.

Coupland ‡ describes a primary carcinoma of the first part of the duodenum which grew into and entirely replaced the gall-bladder. Inasmuch as primary carcinoma of the first part of the duodenum is much rarer than carcinoma of the gall-bladder, it is quite reasonable to raise the question whether the growth did not arise in the gall-bladder.

In rare instances a fistulous passage is established between the gall-bladder and the pyloric end of the stomach; the growth has been known to invade the abdominal wall, then to set up an abscess, and even to lead to an external fistula.

Pressure Effects.—When the growth involves the pylorus, it may lead to pyloric obstruction, and so clinically simulate carcinoma of that part of the stomach. From the anatomical relations of the gall-bladder to the pylorus this is more likely to occur when the growth is near the neck of the gall-bladder.

Rabé and Rey § found the fundus of a carcinomatous gall-bladder firmly adherent to the first part of the duodenum, which was greatly narrowed and had led to dilatation of the stomach. The colon was also adherent to the gall-bladder, and the intestinal obstruction which existed in the case was thus partly explained. Lejonne and Milanoff ‖ have recorded a somewhat similar case.

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* Bohnstedt, quoted by Devic and Gallavardin, Rev. de Méd., July, 1901, p. 569.

† Gilbert and Claude: Archiv. général. de Méd., t. clxxv, 1895, p. 513.

‡ Coupland, S.: Trans. Path. Soc., vol. xxiv, p. 103.

§ Rabé and Rey: Bull. Soc. Anat. Paris, 1897, p. 881.

‖ Lejonne and Milanoff: Bull. Soc. Anat. Paris, 1900, p. 133.

The gall-bladder may, in very rare cases, perforate into the peritoneal cavity, or give rise to a localised abscess. The notes of the following remarkable case were communicated to me by Dr. C. D. Green:

The patient was a woman aged sixty-two, with persistent jaundice, malignant cachexia, and an enlarged liver from which there projected a mass of stony hardness about as large as a bantam's egg; she was suddenly seized with acute abdominal pain, and the hard mass could no longer be felt, but was replaced by a general boggy feeling. Death followed in a few hours from peritonitis. At the autopsy there was a large carcinomatous mass involving the liver in the region of the gall-bladder, colon, and the stomach. An abscess cavity due to destruction of the growth had ruptured into the peritoneal cavity. No trace of the gall-bladder could be made out; the abscess cavity contained a single large biliary calculus, obviously what had been felt during life.

A localised abscess around a carcinomatous gall-bladder was operated upon during life by Mr. Rushton Parker.* Death occurred ten days later from general purulent peritonitis.

Secondary Growths.—The liver is the organ most frequently affected, being involved in about 50 per cent. of the cases. Not infrequently the tumor grows directly into the right lobe.

In Musser's † 100 cases there were metastases in 55, and in all but one of these the liver was involved—in 52 by metastases, in 2 by direct extension. The abdominal lymphatic glands were involved in 16, the lungs or pleura in 10, the peritoneum in 12.

When the growths are numerous, the clinical aspect of the case becomes that of malignant disease of the liver substance. Secondary growths in the lymphatic glands may compress the bile-ducts and portal vein, thus setting up jaundice and ascites. Secondary growths may occur in other abdominal lymphatic glands, in the peritoneum, in the ovaries, and in the lungs.

Infection may travel up from the abdomen into the chest along the lymphatic vessels, which pass immediately behind the sternum to the glands in the anterior mediastinum. A tumor may thus project from the surface of the chest even before the primary growth has been detected.

Beadles ‡ described a case of primary carcinoma of the gall-bladder with a secondary growth as large as a cocoanut arising near the second rib on the right side. In a case of S. West's § the clinical symptoms were those of mediastinal tumor, which at the autopsy was shown to be secondary to a growth in the gall-bladder.

In rare instances the lymphatic glands above the clavicle may be enlarged and readily palpable during life. To this phenomenon of intra-abdominal disease the term "Virchow's gland" has been applied. In cases where acute cholecystitis supervenes in a carcinomatous gall-bladder enlargement of lymphatic glands in the neighbourhood may be inflammatory and not necessarily due to new-growth.

The liver may be healthy, but usually it is enlarged, either from distension with bile or from the presence of secondary growths. In many cases the growth extends directly into the substance of the right lobe, and, as pointed out elsewhere, the tumor may resemble a primary massive carcinoma of the liver. From infection of the bile-ducts suppuration may occur in the liver and give rise to miliary abscesses. In 60 cases tabulated by Winton [*] 4 showed miliary abscesses.

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* Brit. Med. Journ., 1899, vol. ii, p. 1544.

† Musser: Boston Medical and Surgical Journ., vol. cxxi, 1889.

‡ Beadles, C. F.: Trans. Path. Soc., vol. xlviii, p. 119.

§ West, S.: Path. Soc. Trans., vol. xxxvii, p. 144.

ETIOLOGY.

Relation of Primary Carcinoma of the Gall-bladder and Gall-stones.—Special interest attaches to the association of gall-stones and carcinoma of the gall-bladder, inasmuch as the calculi are generally thought to be the cause, whether by direct irritation or otherwise, of the neoplasm. That calculi are commonly met with in primary carcinoma of the gall-bladder is shown by numerous statistics. In Musser's 100 cases gall-stones were stated to be present in 69, and in only three instances was cholelithiasis definitely stated to be absent. Fütterer [†] estimated that calculi were present in 70 per cent.; Winton [‡] in 81 per cent.; Zenker [§] in 85 per cent.; Courvoisier [‖] in 91 per cent.; Siegert in 95 per cent. Janowski [**] in 40 cases of malignant disease of the gall-bladder records calculi in all. Conversely, it appears that primary carcinoma of the gall-bladder occurs in from 14 per cent. to 4 per cent. of all cases of cholelithiasis.

Schroeder [††] estimated that 14 per cent. of persons with cholelithiasis eventually became the subjects of carcinoma of the gall-bladder; in 141 cases of gall-stones there were 20 of primary carcinoma. In 149 cases of gall-stones abstracted from the postmortem records of Guy's Hospital by Keay [‡‡] there were 17 cases of carcinoma of the gall-bladder or cystic duct, or 11.4 per cent. Riedel [§§] estimated the percentage of primary carcinoma in cholelithiasis at from 7 to 8 per cent. Among 242 cases of gall-stones at St. George's Hospital there were 10 cases of primary carcinoma of the gall-bladder, or 4.1 per cent.; this low percentage is possibly accounted for by the fact that in many instances minute bilirubin-calcium calculi were the only ones present. In twenty-one and one-half years there were at St. George's 16 cases of primary carcinoma of the gall-bladder; 13, or 81 per cent., of which were associated with gall-stones.

It has, however, been suggested that the calculi are secondary to the growth, and are the result of obstruction to the passage of bile or of other changes set up by the growth of carcinoma in the gall-bladder. Experimentally, however, it does not appear that bile is more likely to crystallise on stagnation, provided the gall-bladder is aseptic (Mignot [‖‖]). If calculi were the result of obstruction pure and simple, they would be found more frequently in carcinoma of the bile-ducts, where there is much more biliary obstruction than in malignant disease of the gall-bladder. But they are less frequent in the former condition, being present in 23 out of my 62 cases, while in carcinoma of the gall-bladder the percentage is about 90. Besides directly obstructing the exit of bile and mucus from the gall-bladder, a growth in its wall might interfere with its contractions. Both these conditions would lead to biliary stagnation and so favour microbic infection, cholecystitis, and the production of calculi. Further, it is conceivable that the presence of a growth or its disintegration might modify the secretion from the mucous membrane of the gall-bladder.

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[*] Winton, W. B.: Unpublished Thesis for M. D., Cambridge, 1902.

[†] Fütterer, G.: Ueber die Aetiologie der Carcinoms, Wiesbaden, 1901.

[‡] Winton, W. B.: Thesis for M.D., Cambridge, unpublished, 1902.

[§] Zenker, H.: Deutsch. Archiv f. klin. Med., Bd. xliv, S. 159, 1891.

[‖] Courvoisier: Path. u. Chirurg. der Gallenwege, 1890.

[**] Janowski: Ziegler's Beiträge, Bd. x, S. 449, 1891.

[††] Schroeder: Quoted by Keay.

[‡‡] Keay: Medical Treatment of Gall-stones, p. 67.

[§§] Riedel: Berlin. klin. Wochen., 1901, S. 1.

[‖‖] Mignot: Archiv. général. de Méd., 1898, Aug.–Sept.

In this connexion it is important to bear in mind that the cholesterin is derived from the mucous membrane of the gall-bladder, and not from the bile itself. Siegert [*] tried to settle the question whether the presence of a growth in the gall-bladder gave rise to the formation of calculi by a comparison of the incidence of calculi in primary and in secondary carcinoma of that viscus. In 99 cases of primary disease calculi were present in 94; while in 13 cases of secondary growths in its wall they were present in only 2. In 13 other cases of secondary growths that I have collected or seen, calculi were present in one; so in these 26 cases of secondary growths in the gall-bladder gall-stones occurred in 3, or 11.7 per cent., which are within the limits, 5 to 12 per cent. (Schroeder and Naunyn [†]), of the incidence of gall-stones in ordinary routine post-mortem work. These figures, as far as they go, do not support the view that the presence of a growth in the gall-bladder is a factor of any importance in the production of gall-stones. It must, however, be admitted that the presence of a secondary growth in the gall-bladder is not quite the same as a primary growth, especially as regards its relation to the mucous membrane. A secondary growth usually starts under the serous coat, and need not involve the mucous coat, which produces cholesterin, while a primary carcinoma is due to changes in the mucous membrane itself.

There is undoubtedly a very definite relation between cholelithiasis and the development of primary carcinoma of the gall-bladder. But gall-stones are so commonly present without carcinoma developing, that though they dispose to its occurrence, some additional factor is necessary. Possibly the part played by calculi is that of preparing the soil for the direct cause, whatever it may be, of carcinoma. That gall-stones may dispose to fresh attacks of cholecystitis is undoubted, and by thus reducing the resistance of the gall-bladder they may be an indirect cause of carcinoma. The walls of a carcinomatous gall-bladder may show definite evidence of chronic inflammation, and even of calcareous infiltration.[‡] On the other hand, gall-stones are due to catarrh of the mucous membrane of the gall-bladder, and it might be suggested that cancer and gall-stones are both the results of forms of irritation which have much in common.

To sum up, gall-stones are present in the great majority of cases of primary malignant disease of the gall-bladder, while carcinoma develops in from 14 to 4 per cent. of cases of cholelithiasis. It appears that the antecedent of the two conditions is cholelithiasis, and that carcinoma *per se*, whether local in the gall-bladder or present elsewhere in the body, does not set up cholelithiasis. At the present time the questions whether carcinoma is due to a parasite or to the cells of the affected organ having acquired a habit of growth and continued proliferation are unsettled; but from either point of view gall-stones would appear to be favourable to the morbid process. (1) Thus their presence would reduce the resistance of the organ and so dispose to local infection with the hypothetical parasite of carcinoma. (2) While on the non-parasitic theory, gall-stones would irritate the epithelial lining of the gall-bladder and keep up the habit of proliferation, which, under favourable conditions, viz., diminished resistance of the underlying tissues, may become carcinomatous.

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[*] Siegert: Virchow's Archiv, Bd. cxxxiii, S. 353.

[†] Schroeder: Quoted by Naunyn, who accepts this estimate, On Cholelithiasis, p. 40. Translated by New Sydenham Soc.

[‡] Beadles, C. F.: Trans. Path. Soc., vol. xlvii, p. 69.

In connexion with the close association between carcinoma of the gall-bladder and cholelithiasis the rarity of a similar association between renal calculi and growths of the pelvis of the kidney is of interest. It must be remembered that both renal calculi and new-growths of the renal pelvis are less common than gall-stones and carcinoma of the gall-bladder.

Kelynack[*] refers to 23 examples of associated renal calculus and growth. In 8 cases of papilloma of the pelvis of the kidney collected by Drew[†] calculi were present in 4. The causal relationship of the irritation of a calculus to a villous growth of the renal pelvis would reasonably be much more probable than to malignant disease of the substance of the kidney.

Sex.—Malignant disease of the gall-bladder is very much commoner in women. According to Fütterer's figures (202 females, 52 males), it is four times more often seen in the female sex. Musser's cases included 75 females and 23 males (or 3 to 1); Siegert's, 79 females and 14 males (5½ to 1); while Ames gives the proportion of females to males as 4 to 1; Courvoisier, as 5 to 1. In 50 cases of Terrier and Auvray,[‡] 40 were women and 10 men. In Winton's 60 cases 43 were females and 17 males (4 to 1).

This predominance of females in carcinoma of the gall-bladder corresponds to their greater liability to gall-stones, which is calculated by Schroeder in the proportion of 5 to 1, by Murchison 3 to 2, Bouchard 100 to 66, Harley 2 to 1. The overwhelming majority of female patients among the subjects of gall-bladder carcinoma contrasts with the sex incidence in carcinoma of the bile-ducts; thus in 18 cases Musser found the sexes equally represented, and in my 75 cases 44 were males and 31 females. In this connexion it may be mentioned that gall-stones are less frequently associated with carcinoma of the bile-ducts; thus in Musser's 18 cases they were present in 11, and in my 62 cases 23, times.

The pressure of the corset on the liver may, as suggested by Fütterer,[§] increase the friction between calculi and the walls of the gall-bladder, and so may help to explain the great predominance of females in primary carcinoma of the gall-bladder. In this connexion it is remarkable that the bile-ducts, which can hardly be affected in the same way by the wearing of a corset or belt, are more often the subject of carcinoma in men than in women. Graham recorded a case of carcinoma of the gall-bladder in a shoemaker whose last pressed upon the liver much as a corset might do, and Fütterer is inclined to think that pressure of this kind may be a factor in the male cases.

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[*] Kelynack, T. N.: Renal Growths, p. 27.
[†] Drew, D.: Trans. Path. Soc., vol. xlviii, p. 133.
[‡] Terrier and Auvray: Rev. de chirurg., 1900, p. 143.
[§] Fütterer, G.: Chicago Medical Soc., April 1, 1897.

While primary carcinoma is much commoner in women, Siegert's statistics of secondary growths in the bladder, though only 13 in number, showed that the male sex were affected in 10, or 77 per cent., and the female sex in 3, or 23 per cent.

Age.—Frerichs described the disease as one of old age. In 17 cases collected by Villard 9 were over seventy years of age. The average age of Fütterer's large series was fifty-eight years, and curiously enough the average age was the same in 60 cases collected by Winton, many of them from the unpublished records of St. George's and other hospitals. Carcinoma of the gall-bladder is very rare before forty years of age. Markham * described an exceptional case in a woman aged twenty-eight. At the other extreme the most advanced age was ninety (Thomas and Noica †).

CLINICAL PICTURE.

In considering the clinical aspect of malignant disease of the gall-bladder it may be well at the outset to point out that the clinical manifestations are roughly divisible into three groups: (i) Those symptoms connected with pre-existing cholelithiasis; (ii) the local effects of malignant disease of the gall-bladder; (iii) complications due to invasion of adjacent parts by the tumor and to secondary growths in the liver, peritoneum, and elsewhere.

The patient, as has already been pointed out, is generally a woman between fifty and sixty years of age, who may have suffered from symptoms of gall-stones. Biliary colic may closely precede the development of carcinoma, but in some instances there is a very long interval between the first appearance of colic and the development of carcinoma.

Jourdan ‡ recorded a case where the colic began twenty-five years before the growth appeared. Bret § describes a case where a woman, who died at the age of thirty-six with carcinoma of the gall-bladder enclosing an oval calculus, had had biliary colic since the age of twenty.

There is often, however, no history of gall-stone colic in fatal cases of carcinoma of the gall-bladder; the calculi may remain latent in the gall-bladder and never pass into the ducts. Kehr ‖ says that clinical evidence of cholelithiasis is wanting in the majority of the victims of carcinoma of the gall-bladder. In other instances pain really due to inflammation or adhesions around the gall-bladder is regarded as dyspepsia.

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* Markham: Trans. Path. Soc., vol. viii, p. 243.
† Thomas and Noica: Bull. Soc. Anat. Paris, 1896, p. 471.
‡ Jourdan: Bull. Soc. Anat. Paris, 1891, p. 323.
§ Bret: Lyon Médical, tome lxxxix, p. 35, 1898.
‖ Kehr: Diagnosis of Gall-stone Disease, p. 92, American translation.

Usually the first thing noticed by the patient is a feeling of discomfort and heaviness in the right hypochondrium and parts around. According to Head,* the eighth dorsal segment is the visceral area in connexion with the gall-bladder. This may be followed by loss of appetite, gastro-intestinal disturbance accompanied with definite pain, and even by attacks of colic, indistinguishable from biliary paroxysms. A tumor may be felt in more than half the cases in the situation of the gall-bladder, which is at first smooth and oval, like the gall-bladder, and subsequently becomes hard, irregular, and may be tender. Like the liver, it moves with respiration unless fixed by adhesions. The tumor may reach the size of a cocoanut. These may be called the local manifestations, and, on the whole, resemble those of cholelithiasis. As time goes on the growth invades neighbouring parts, and secondary growths may spring up; additional, or what may be called secondary, symptoms, are thus produced. Carcinoma of the gall-bladder may remain latent until the secondary growths set up prominent symptoms. This is well illustrated by the following case:

A man aged sixty-eight was in St. George's Hospital with ascites, but no jaundice, and was diagnosed as cirrhosis. At the autopsy there was a primary columnar-celled carcinoma of the gall-bladder, which contained gall-stones. The liver was directly invaded by the growth, and there was a large, broken-down growth in the glands behind the pancreas, which compressed the portal vein.

When the liver becomes infiltrated with secondary growths, the clinical aspect of the case may become that of carcinoma of the liver. Enlargement of the liver can be made out in about half the cases, but it may be obscured by ascites or by flatulent distension. The surface may be smooth when the enlargement is due to distension with bile, nodular from secondary growths, or there may be a definite tumor mass formed by the cancerous gall-bladder and the adjacent liver substance infiltrated by growth. The bile-ducts may also become invaded by direct extension of the growth or by pressure exerted from without by secondary growths or by enlarged glands, situated either in the portal fissure or in the neighbourhood of the pancreas. Jaundice is thus set up, and the symptoms are much the same as those of primary carcinoma of the head of the pancreas or of the bile-ducts. Though not a necessary result of carcinoma of the gall-bladder, jaundice is very frequent. In 30 cases collected by Meunier † it was absent in only four. In Winton's 60 cases permanent jaundice occurred in 33, or 55 per cent., and in 69 per cent. of Musser's 100 cases.

As Mayo Robson ‡ points out, jaundice may be due to catarrh of the ducts, but in that event it would not have the progressive character met with in malignant disease, but would tend to vary or even pass away. I have seen several cases of carcinoma of the gall-bladder in which jaundice came on after vomiting and diarrhœa, the characters of catarrhal jaundice, but persisted until death, and at the postmortem examination was found to depend on definite obstruction to the ducts. In such cases the onset was probably catarrhal, but obstruction supervened and rendered the icterus permanent.

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* Head, H.: Brain, part lxi, p. 75.

† Meunier: Bull. Soc. Anat. Paris, 1893, p. 585.

‡ Mayo Robson: Brit. Med. Journ., 1897, vol. i, p. 710.

The following case illustrates this point, and also the latency of gall-stones in carcinoma of the gall-bladder:

A jaundiced woman, aged forty-six years, was under my care in St. George's Hospital in 1897. Two months before her death she was attacked with sickness and pain after food without any sufficient cause; this lasted for one week and was followed by jaundice, which persisted until her death. She was quite certain that there had been no biliary colic at any time. Her health had generally been very good and there had been no dyspepsia. She was a wasting but not emaciated woman, with the remains of good looks. There was marked jaundice, but no itching or eruption of the skin. The pulse was 90. The fæces were pale and the urine contained bile. The liver was much enlarged, but the gall-bladder could not be made out. The umbilicus was brown and hard; this was noticed directly after the onset of jaundice. There was no ascites. A movable tumor the size of one's hand was palpable in the left inguinal region. The patient was in the hospital a month, during which time she steadily got weaker; a week before death there was hæmorrhage from the umbilicus, and on the two days preceding death hæmorrhage from the bowel. She died in a sleepy state. At the autopsy there was a primary spheroidal-celled carcinoma of the gall-bladder, which contained numerous pearl-like calculi and three large calculi, one of which had undergone spontaneous fracture,* probably some time before death. The liver weighed 11 pounds 3 ounces, and contained numerous secondary growths. The portal vein and the common bile-duct were embedded in secondary growth and narrowed. There was, however, no ascites. There was a large loose growth in the great omentum, corresponding to the movable tumor felt during life. There were dilated veins in the rectum and a small ulcer from which the hæmorrhage must have come.

Jaundice may also be due to a gall-stone in the common duct either obstructing it mechanically or setting up intermittent hepatic fever.

Warthin † describes a case of carcinoma of the gall-bladder in which jaundice, leucoderma, and marked pigmentation of the skin, suggesting Addison's disease, were all present. After death secondary growths were found in both adrenal bodies.

Ascites is met with in about one-quarter of the cases. In Winton's 60 cases it was present in 14. It depends not on malignant disease of the gall-bladder itself, but on complications set up by secondary growths or by extension of the primary growth. It may be associated with, but does not necessarily follow, pressure on the portal vein; and is most satisfactorily explained by chronic peritonitis set up by secondary growths on the surface of the peritoneum. When there are numerous growths in the peritoneum, the effusion may be fatty as the result of cellular degeneration (chyliform or fatty ascites).

Œdema of the legs may occur in the late stages of cachexia, and be due to cardiac debility, or possibly to the pressure exerted on the inferior vena cava by a large ascitic effusion or by enlarged glands in the neighbourhood. Thrombosis of the inferior vena cava has been recorded.

There is often dyspepsia, which in a few instances is due to a definite organic cause—viz., obstruction at the pylorus from invasion of the growth, and may then be associated with a dilated stomach. There may be vomiting, flatulent distension of the abdomen, and usually constipation. In some instances diarrhœa alternates with constipation. Extension of the growth to the colon may give rise to chronic obstruction or eventually to complete intestinal obstruction. When deep jaundice has developed, the patient gradually passes into the condition of cholæmia. The temperature is normal or subnormal unless there are complications. Muscular wasting and loss of strength steadily develop, and eventually emaciation, exhaustion, and cachexia become marked; the biliary toxæmia gives rise to hæmorrhages, petechiæ, epistaxis, and occasionally hæmatemesis and melæna, mental failure, delirium, coma, and death. Terminal infections may take place and carry the patient off, and this without the temperature being necessarily raised.

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* Trans. Path. Soc., vol. xlix, p. 135.

† Warthin: Philadelphia Medical Journal, July 7–14, 1900.

Complications.—The gall-bladder may in rare instances perforate into the peritoneal cavity and set up peritonitis. The growth may extend and perforate into the transverse colon, and, as a result, the gall-bladder may become infected and an abscess, either in the gall-bladder or in its immediate neighbourhood, may result.* Suppurative cholangitis may occur and spread into the liver, the gall-bladder, or Wirsung's duct, and in the latter event set up acute suppurative pancreatitis. Pus may collect in the gall-bladder, either when the growth is in a very early stage (*vide* p. 602), or when there are numerous secondary growths.

In a man aged fifty-two, whom I examined after death at St. George's Hospital, the gall-bladder was the site of a primary spheroidal-celled carcinoma which had given rise to numerous secondary growths in the liver, which, with the stomach, weighed 15 pounds. There were calculi and pus in the gall-bladder. There was a chyliform (fatty) effusion into the left pleura and the peritoneum.

A local peritoneal abscess may form close to a carcinomatous gall-bladder, or there may be circumscribed acute peritonitis in the neighbourhood of the growth, due to microbic infection.

This was present in a woman aged forty-five years upon whom exploratory laparotomy was performed by my colleague, Mr. Jaffrey, for a large tumor in the hepatic region. A quantity of fibrin was found around a carcinomatous mass in the position of the gall-bladder, enclosing two calculi.

In cases where cholecystitis supervenes in a carcinomatous gall-bladder micro-organisms may be absorbed and give rise to infection elsewhere in the body. Lorrain † has reported a case of lithiasis and carcinoma of the gall-bladder, with cholecystitis, and endocarditis. Pyloric obstruction and obstruction of the transverse colon due to direct extension of growth have been already referred to.

Duration.—There is some difficulty in determining the duration of the disease, since the early symptoms so closely resemble cholelithiasis, with which it is almost always combined. Probably it remains latent for a considerable time, but when jaundice and cholæmia have set in, the end is near. Some cases die very soon after the appearance of definite symptoms. On the whole, perhaps, the average duration of the disease may be put down as less than six months.

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* Blanc and Leray: Bull. Sóc. Anat. Paris, 1897, p. 69.

† Lorrain: Bull. Soc. Anat. Paris, 1903, p. 527.

DIAGNOSIS.

The presence of a hard, nodular, progressively increasing tumor in the position of the gall-bladder in a patient about the age of fifty years, especially in a woman, is suggestive of the disease. Dull pain, loss of appetite, and wasting are in favour of growth. When secondary growths can be felt in the liver or in the supraclavicular fossæ, the diagnosis is practically clinched.

The only fallacy is, of course, that there is a primary growth somewhere else which has given rise to generalisation, and that among other places a secondary growth has developed in or close to the gall-bladder. Careful search for any primary growth in the stomach, rectum, œsophagus, breast, and uterus should, therefore, always be made.

Jaundice is not an early symptom, though it is true the diagnosis is often not made until it appears.

Differential Diagnosis.—*From Gall-stones.*—Malignant disease, especially in the earlier stages, when the growth is confined to the gall-bladder, is very like cholelithiasis, and since in the vast majority of the cases carcinoma develops subsequently to gall-stones, it is very difficult to say when malignant disease has begun. The enlargement of the gall-bladder is in favour of growth, especially if it is progressive and nodular. On the other hand, extensive inflammatory thickening of the walls of the gall-bladder may closely simulate new-growth, even when the parts are exposed during laparotomy, and this impression may be supported when the thick-walled viscus is punctured.

In a case under my care which was operated upon by Mr. Warrington Haward in 1896 a piece of tissue of doubtful nature was removed, and before the end of the operation, during which 117 calculi were removed, microscopic examination showed that the tissue was inflammatory.

An inflamed gall-bladder may clinically appear of stony hardness either from contained calculi, or, more rarely, from secondary calcification of its walls. In addition to this the occurrence of dense adhesions to the surrounding parts—colon, stomach, omentum, etc.—and inflammatory enlargement of glands in the portal fissure, lesser omentum, and around the common bile-duct, where it passes into relation to the pancreas, may all suggest, even when the abdomen is opened, that there is malignant disease either of the gall-bladder, pylorus, or colon; and that secondary growths in the glands, by pressure on the ducts, have given rise to jaundice. The presence of gall-stones in the common duct may simulate glands invaded by carcinoma.

In any case of doubt the gall-bladder should be opened and not merely punctured. The difficulties of diagnosing between cholelithiasis and carcinoma of the gall-bladder are well illustrated by two cases of Mr. Mayo Robson's.*

"In a doubtful case of this kind in a woman of fifty I opened the abdomen and found what appeared to be a malignant tumor of the gall-bladder, which was punctured in several spots with an exploring syringe; finding it firm and hard, I

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* Mayo Robson: The Medical Press and Circular, April 21, 1897, p. 407.

> concluded it was malignant, and as it was too extensive for removal, I closed the abdomen, thinking nothing more could be done. The patient, however, forthwith recovered and is now well, with no remnant of her tumor. It is, of course, impossible to say that this was not cancer, but in all probability it was an inflammatory swelling associated with gall-stones.
>
> "In another case of tumor where there was a suspicion of malignancy I opened an abscess of the liver containing 30 gall-stones, giving marked relief, though only for a time, as death supervened four months later, when malignant disease was found."
>
> In the second case carcinoma had probably developed at the time of operation.

As time goes on the cachexia, the presence of increasing jaundice, and, most positive evidence of all, secondary growths, may appear and strengthen or decide the diagnosis.

From Malignant Disease of the Liver.—In the later stages, when the liver is enlarged and presents either a large tumor or several small ones, the diagnosis from primary or secondary malignant disease is often very difficult or even impossible. The history of gall-stones would suggest that the primary growth might have started in the gall-bladder, and the original appearance of a tumor in that situation would strengthen the diagnosis in the absence of any evidence pointing to primary carcinoma of the stomach, colon, etc. Unfortunately, a history of gall-stones is often absent, while a tumor in the position of the gall-bladder is felt only in about half the cases.

In rare instances *syphilitic disease* of the liver may imitate malignant disease of the gall-bladder. From cicatricial contraction and deformity a piece of the right lobe may become elongated and hard and be thought during life to be a carcinomatous gall-bladder. (Gerhardt.*)

Carcinoma of the Stomach.—When the cancerous gall-bladder gives rise to pyloric obstruction, it may naturally be regarded as carcinoma of the pylorus. There is an absence of the movable pyloric tumor, but, unfortunately, this may also occur in true pyloric cancer. The history of gall-stones and the presence of jaundice point to a biliary origin for the stomach symptoms.

Hartmann † suggests that when doubt exists as to the position of a tumor, whether in the gall-bladder or the pylorus, the following means may be employed. The situation of the tumor is first accurately determined; the stomach is then distended with gas by means of an effervescing mixture. If the tumor remains in the same position as before, it is the gall-bladder; if it be found to have moved under the ribs, it is pyloric.

Carcinoma of the transverse colon in the neighbourhood of the gall-bladder may closely resemble carcinoma of the gall-bladder.

Cancer of the bile-ducts and of the head of the pancreas may be simulated by those cases of gall-bladder carcinoma in which jaundice occurs early. In the former conditions the gall-bladder is more often distended and smooth, while in the latter the tumor is hard and solid, and may be irregular, and the liver is more likely to be enlarged and show secondary growths. The question of diagnosis between these two conditions is discussed at greater length on page 693. In malignant disease of the pancreas a tumor may sometimes be felt deeper in the abdomen and close to the spine.

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* Gerhardt: La Sem. Méd., 1898, p. 273.

† Hartmann: Soc. Chirurg. Paris, Oct., 1899.

Tumors arising from the parts around the gall-bladder, such as a hydatid cyst, a floating kidney, or renal tumor on the right side, or more rarely a tumor of the right suprarenal body, may imitate carcinoma of the gall-bladder; or one of these conditions may be diagnosed when the growth is really in the gall-bladder.

In a man aged seventy-nine years who presented a rounded, tender tumor the size of an apple in the right hypochondrium, without jaundice or ascites, the diagnosis lay between a calcified hydatid cyst and carcinoma of the gall-bladder. At the autopsy there was a columnar-celled carcinoma of the gall-bladder with miliary abscesses in the liver.*

When a *floating kidney* gives rise to jaundice by traction or pressure on the bile-ducts, the clinical aspect may closely resemble that of cholelithiasis or malignant disease of the gall-bladder. The free mobility of a floating kidney and the fact that it can be displaced from continuity with the liver are points that should prevent its being regarded as disease of the gall-bladder. The lumbar region should be carefully examined, and the abdomen should be palpated in the knee-and-elbow position.

Under certain conditions *fæcal accumulation* in the transverse colon may, by the colicky pains and the presence of numerous hard masses in the neighbourhood of the gall-bladder, suggest carcinoma of the gall-bladder with secondary growths around. Examination under an anæsthetic may reveal the fact that these masses can be indented by the finger, and subsequent examination that they vary in position and in number. In such cases the effect of purgatives and massage should be tried.

PROGNOSIS AND TREATMENT.

The prognosis and treatment may be considered under two heads: (1) From a medical, and (2) from a surgical, point of view.

The disease being necessarily fatal unless it can be removed, medical treatment is merely palliative, and resolves itself into the relief of pain and discomfort by morphia and opium, lessening vomiting and nausea by bismuth, hydrocyanic acid, and morphia, combating constipation and preventing intestinal fermentation by calomel, other preparations of mercury, salol, or various antiseptic remedies. Under such treatment the prognosis is of the gloomiest.

Surgically, if the growth be removed and there are no secondary growths, the prognosis should be more hopeful.

In their tabular statement of the statistics of operations on the gall-bladder Terrier and Auvray † record—(i) 16 cases in which the gall-bladder was removed for malignant disease with an operation mortality of 31.25 per cent.; and (ii) a further series of 18 cases in which, in addition to removal of the gall-bladder, part of the liver was resected. Of these 18 cases 3, or 16.7 per cent., died as the immediate result of the operation.

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* Lejonne et Melanoff: Bull. Soc. Anat. Paris, 1900, p. 133.

† Terrier and Auvray: Chirurgie du Foie, p. 303, 1901.

The high mortality from operation mainly depends on hæmorrhage, which occurs so readily in cases of chronic jaundice. Thus there may be constant oozing from the wound, and after death extensive hæmorrhagic infiltration may be found around the ducts and pancreas. This tendency to hæmorrhage should always be guarded against as far as possible by giving large doses of chloride of calcium to jaundiced patients before operation. Calcium chloride does not always prevent hæmorrhage in jaundiced patients, and it is possible, as suggested by Berg,* that degeneration of the vessel-walls is responsible for the hæmorrhagic tendency, either in addition to or instead of diminished coagulation power of the blood.

After recovery from operation a biliary fistula is sometimes left. In some instances there is temporary improvement after resection of the gall-bladder, but in nearly all cases a recurrence of the growth occurs within six months. The only exception to this in Terrier and Auvray's statistics is Hochenegg's † case, which survived cholecystectomy with partial resection of the liver for three years. Mayo Robson's ‡ case, in which a similar operation was performed, recovered completely. Warren § performed a similar operation for carcinoma of the cystic duct with recovery. The following case illustrates the extreme malignancy of primary carcinoma of the gall-bladder, even when removed in a very early stage and apparently under the most favourable conditions.

Heidenhain, ‖ in the course of an operation on the gall-bladder for the removal of six calculi, noticed a small, button-like thickening in its wall and removed the gall-bladder; microscopic examination showed that it was carcinomatous. Three months later the patient died from growths in the liver, though at the operation it appeared perfectly healthy.

The success of the operation depends on early operation and on the absence of secondary growths, and this cannot be positively excluded before the abdomen has been opened.

The diagnosis of carcinoma of the gall-bladder being difficult, cases occur in which laparotomy is undertaken with a view of relieving cholelithiasis, and carcinoma of the gall-bladder is found perhaps in an early stage. Such early cases are the most favourable for cholecystectomy, and the prognosis is less gloomy than in more advanced cases.

According to Carl Beck,** forty per cent. of the cases operated upon for cholelithiasis are found to show carcinoma of the gall-bladder.

SECONDARY MALIGNANT DISEASES OF THE GALL-BLADDER.

Secondary growths occasionally occur in the course of widespread carcinoma or more rarely in widely disseminated sarcoma. The growths are usually situated either on the peritoneum, as in cases of extensive malignant disease of the peritoneum, or just under the peritoneal covering of the gall-bladder. The growths very rarely invade the mucous coat of the gall-bladder, and, as shown by Siegert's * and my own figures (*vide* p. 628), are not specially related to the presence of gall-stones. Another way in which secondary malignant disease contrasts with primary malignant disease of the gall-bladder is in the sex incidence: whereas primary carcinoma is about four times commoner in women, secondary growths were much more frequent in the male sex in Siegert's figures. As a rule, secondary growths do not obstruct the cystic duct, but this may, of course, occur and give rise to hydrops of the gall-bladder. Growths of the stomach, colon, etc., may spread into the gall-bladder.

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* Berg: Annals of Surgery, 1903, p. 356.

† Hochenegg: Wiener klin. Wochen., 1890.

‡ Mayo Robson: Medico-Chirurg. Trans., vol. lxxix, p. 159, and Diseases of Gall-bladder, 3d ed., p. 186.

§ Warren: Boston Med. and Surg. Journ., March 15, 1900, p. 276.

‖ Heidenhain: Verhandl. d. deutsch. Ges. f. Chirurg., 1898, S. 126.

** Beck, C.: The Medical Week, 1897, p. 137.

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* Siegert: Virchow's Archiv, Bd. cxxxiii, S. 353.

DISEASES OF THE BILE-DUCTS.

ABNORMALITIES OF THE BILE-DUCTS.

Atresia or complete obliteration of any part of the bile-ducts is pathological, and usually due to inflammatory changes occurring in fœtal life. The cystic duct is an exception to this general statement, as it is frequently obliterated by inflammation spreading from cholecystitis and is often the result of the ulceration and cicatrisation in later life, associated with gall-stones. Simple stricture and obstruction by pressure from without, or by new-growths in the walls, by gall-stones, parasites, etc., are described elsewhere. Abnormalities in the ducts chiefly consist in variation in the length of the cystic and common bile-ducts, and in the presence of abnormal communications between the gall-bladder and the liver (hepatocystic ducts). The left and right hepatic ducts may remain separate for a considerable distance, and only join when the cystic duct unites with them; in such cases there is no common hepatic duct. The cystic duct may not join the common hepatic duct until close to the duodenum, so that the common bile-duct is very short. In cases of true congenital absence of the gall-bladder (*vide* p. 589) the common bile-duct may be dilated in part of its course.

Variations in the method of opening of the common bile-duct into the duodenum exist; Letulle and Nattan-Larrier,* in their description of the Vaterian region, or portion enclosing the biliary papilla, of the duodenum, have described four types of the openings of the common bile- and Wirsung's ducts. In some instances the common bile-duct opens into the duodenum separate from the main pancreatic duct. It very occasionally opens with the accessory pancreatic duct of Santorini, the main pancreatic duct being quite separate and opening alone in the position of the normal biliary papilla. In 104 cases Schirmer † found this four times.

The effect of tight lacing on the biliary apparatus is referred to elsewhere (p. 15).

CONGENITAL OBLITERATION OF THE BILE-DUCTS.

Definition.—Obliteration of the bile-ducts is usually due to a descending inflammation, which is secondary to intra-uterine cirrhosis of the liver; in a few instances, however, the obliteration may possibly depend on fœtal peritonitis. There is severe obstructive jaundice, which passes into cholæmia and is accompanied by numerous hæmorrhages; life is very seldom prolonged beyond six months.

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* Letulle and Nattan-Larrier: Bull. Soc. Anat. Paris, 1899, p. 987.

† Schirmer: Inaug. Diss., Basel, 1893.

Nomenclature.—Most of the cases are associated with cirrhosis, and since, as will be seen later, it is probable that the cirrhosis is the primary change and the cholangitis and obstruction of the ducts a secondary and later result, the term "congenital hepatic cirrhosis with obliterative cholangitis" describes the condition more accurately. But since congenital obliteration may possibly be brought about in other ways, it is better to retain the more familiar and inclusive title of congenital obliteration of the bile-ducts. Our knowledge of this rare and interesting disease is chiefly due to Dr. John Thomson, of Edinburgh.

Incidence.—In 1892 Thomson's[*] monograph, containing 50 cases, appeared. I have notes of 14 additional cases,[†] which do not include cases of idiopathic dilatation of the common duct, some of which may depend on the same or on an allied process.

Treves' case[‡] was successfully operated upon at the age of nineteen years for jaundice of sixteen years' duration, and obliteration and absence of the lower end of the bile-duct were found. It differs so markedly from all the other cases that it is doubtful whether it belongs to the same category. Jaundice did not begin until the age of three years, instead of either at or shortly after birth. Possibly, though Treves does not suggest it, the obliteration of the duct was due to the effects of a calculus lodging in the duct or at about the time of the onset of jaundice. Thomson[§] considers that the same morbid process is at work in cholelithiasis in infants as in congenital obliteration of the bile-ducts, and supports this suggestion by quoting two cases of infantile cholelithiasis in which the biliary apparatus was abnormal (Cuffer, Bouisson). Treves' remarkable case may perhaps, therefore, be considered as allied to, if not a very slightly marked example of, the same class.

A remarkable case of Ashby's,[‖] a girl aged seven years who had been jaundiced for two and one-half years, is akin to Treves' case. The common bile-duct was obliterated near the duodenum, but the proximal part, together with the cystic duct, formed an enormous cyst containing sixteen pints of bile-stained mucus.

ETIOLOGY.

Hereditary Influences.—As in other congenital affections, such as deformities, and congenital hypertrophy with stenosis of the pylorus, there is a marked tendency for the disease to occur in members of the same family. As will be pointed out later, a peculiar form of very fatal cirrhosis in Brahmin babies in Calcutta which is a family disease, has a bearing on the pathogeny of congenital obliteration of the bile-ducts. It is possible that Arkwright's[**] series of 14 cases, with 4 survivors, in one family, of dangerous icterus neonatorum belonged to this group of congenital obliteration of the bile-ducts.

Association with Malformations.—There does not seem to be any real association between malformations and this disease. Concomitant deficiencies in the liver must be regarded as part of the disease, and not as true malformations.

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[*] Thomson, J.: Congenital Obliteration of the Bile-ducts, 1892.

[†] These cases are those of Heneage Gibbes, Giese, J. L. Steven, Kynock, F. H. Hawkins, Putnam, Ross, Rolleston and Hayne, Wollstein, G. Parker, Still, and Menzies. The references are given at the end of the paper.

[‡] Treves: The Practitioner, Jan., 1899, p. 18.

[§] Thomson, J.: Edinburgh Hospital Reports, vol. v, p. 1, 1898.

[‖] Ashby: Medical Chronicle, Oct., 1898, p. 28.

[**] Arkwright, J. A.: Edinburgh Med. Journ., Aug., 1902.

Witzel's * case of a number of true malformations and obliteration of the ducts probably belongs to the group of cases of congenital cystic disease of the liver. (*Vide* p. 445.)

In a case of complete absence of the biliary apparatus in an infant one month old there was a congenital malformation of the left upper arm. (Kirmisson and Hébert.†)

Syphilis is not an important and certainly not more than an occasional cause of the change in the ducts and liver. This is shown not only by the histological character of the change in the liver, but by the freedom of the parents and patients from signs of syphilis. Among the parents of Thomson's 50 cases there was evidence of syphilis in only 5 individuals, and in 6, or possibly in 9, of the patients. While there is every reason to believe that syphilis plays no part in the usual type of the cases, it is possible that stricture of the ducts might be due to fœtal peritonitis, which is usually connected with syphilis, or that gummatous inflammation might attack the walls of the ducts, as in Beck's case.‡

Sex.—In Thomson's cases the sex was given in 34, and showed a preponderance of males—21 males, 13 females. In the 14 other cases 7 were females and 7 males, making in all 28 males to 20 females.

PATHOGENY.

John Thomson, in his monograph § on the subject, believed that in the great majority of cases there was, to start with, a congenital malformation of the ducts which narrowed the available lumen. This obstruction to the free exit of bile disposed to catarrh, blocking, and finally to obliteration of the ducts. As a result of the obstruction to the free passage of bile into the duodenum biliary cirrhosis was started. In a later article, contributed to Allbutt's System of Medicine,‖ this writer so far modifies his views as to omit any reference to a primary congenital abnormality as a factor in the condition. The process is regarded as a descending cholangitis set up by toxic bodies in the bile, compared to toluylendiamin; when the disease has gone so far as to interfere with the free passage of bile from the liver, biliary cirrhosis develops, as in Charcot and Gombault's experimental ligature of the bile-ducts in guinea-pigs.**

Ford,†† in a recent paper on obstructive biliary cirrhosis, has collected 24 cases since 1882, in which cirrhosis of the liver was associated with, and, as he believes, due to, obstruction of the common duct. Of these 24 cases, no fewer than 9 are examples of congenital obliteration of the bile-ducts. In fact, his statistical proof that biliary obstruction *per se* induces cirrhosis of the liver rests in some measure on cases of congenital obliteration of the ducts.

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* Witzel, O.: Centralblatt f. Gynäk., 1880, S. 561.

† Kirmisson and Hébert: Bull. Soc. Anat. Paris, 1903, p. 317.

‡ Beck: Schmidt's Jahrb., 1884, S. 204.

§ Thomson: Congenital Obliteration of the Bile-ducts, p. 38.

‖ Thomson: Allbutt's System of Medicine, vol. iv, p. 253.

** Charcot and Gombault: Archives de Physiologie, second series, tome iii, p. 272, 1876.

†† Ford, W. W.: American Journ. of Med. Sciences, vol. cxxi, p. 60, 1901.

It is a point of significant interest that cirrhosis of the liver is comparatively rarely found in association with obstruction of the bile-ducts in adults, and, when present, is usually associated with gall-stones and infection of the ducts (*vide* p. 326), while cirrhosis seems to be a definite accompaniment of congenital obliteration of the ducts.

In J. Thomson's 50 cases a microscopical examination was only made in 10 and in all but one of these it is stated that cirrhosis was present; in 13 other cases that I have notes of cirrhosis was present in at least 12.

The question therefore arises whether there is any evidence to support the theory that cirrhosis in these cases is dependent on the obliteration of the larger bile-ducts. If it can be established that the change in the bile-duct is older and more advanced than in the liver, there is fair ground for regarding the hepatic lesion as due to the obstruction in the ducts. Ross * describes obliteration of the common bile-duct near the duodenum in a female child, aged three months, whose liver showed small-celled infiltration around the bile-ducts rather than fibrosis. In this instance it must be admitted that the evidence points to the change in the bile-duct being the older. On the other hand, in the other cases, as far as one can judge, fibrosis in the liver is quite as old as the lesion in the bile-ducts. Thomson refers to 7 cases of infantile jaundice with symptoms similar to those of congenital obliteration of the bile-ducts, but with pervious ducts; they proved fatal at seventeen days of age on an average instead of at two and one-half months, as in congenital obliteration of the ducts. "This suggests that they are merely earlier cases of the same condition—before the blocking has occurred."†

The following hypothesis appears to be a reasonable explanation of the pathogeny of so-called congenital obliteration of the bile-ducts: In the first instance, poisons pass by the blood from the placenta to the fœtus by the umbilical vein; some of this blood at once passes through the liver, and, in virtue of the toxic effect of the contained body or bodies, induces ordinary portal or multilobular cirrhosis of the liver; the rest of the blood in the umbilical vein passes directly into the general circulation of the fœtus by the ductus venosus, and subsequently, by means of the hepatic artery, will convey the same poison to the liver. By this means the toxic body, which, as Thomson suggests, may be analogous to toluylendiamin, is excreted into the small intra-hepatic bile-ducts and sets up cholangitis and monolobular cirrhosis, like that seen in hypertrophic biliary cirrhosis. In this way a mixed cirrhosis (portal and biliary) is induced. The cholangitis descends to the larger ducts, and gives rise to an obliterative cholangitis—a process analogous to obliterative appendicitis. The difference between this condition of congenital (umbilical) cirrhosis with obliterative cholangitis and other forms of cirrhosis in post-natal life consists in the further change in the large bile-ducts and gall-bladder. An attempt to explain this additional lesion may be made as follows: The bile-ducts are extremely small at birth, and any inflammatory change will, from the small size of the lumen, produce stenosis much more readily than in later life. An analogous effect is seen in the fact that laryngeal obstruction in diphtheria is more frequent in young subjects than in older patients, quite apart from the much greater frequency of the disease in the young. The opposed inflamed surfaces of the bile-ducts will also come in contact more readily, and, as in catarrhal appendicitis, obliteration might result.

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* Ross, D.: Lancet, 1901, vol. i, p. 102.

† Thomson: Congenital Obliteration of the Bile-ducts, p. 30.

The following considerations bear on the hypothesis that the disease is primarily a congenital cirrhosis:

1. The almost constant occurrence of cirrhosis in these cases of bile-duct obstruction in infants as compared with the infrequency and irregularity with which cirrhosis follows obstruction of the larger bile-ducts in later life. The mixed character of the cirrhosis explains the discrepancy in the recorded cases, some authors speaking of biliary, others of multilobular, cirrhosis.

2. The large size of the liver—this resembles hypertrophic biliary cirrhosis. In simple obstruction of the larger bile-ducts in adults the liver, though swollen from retained bile in the early stages, is usually small after death.

3. The large size of the spleen—a phenomenon not met with in uncomplicated biliary obstruction. The large size of the spleen is best explained as the result of toxic bodies reaching the organ by the splenic artery. In congenital syphilis, where it is probable that the poison reaches the liver by the umbilical vein and is derived from the maternal circulation rather than that the ovum is infected by a syphilitic spermatozoön, there is a similar splenic enlargement. In both conditions there is cirrhosis due to poisons arriving by the umbilical vein; the difference between the pericellular cirrhosis of hereditary syphilis and the mixed (monolobular and multilobular) cirrhosis of so-called congenital obliteration of the bile-ducts must depend on a difference in the poisons in the two diseases. This is at one with Thomson's statistical proof that syphilis plays no part in the antecedents of so-called congenital obliteration of the bile-ducts.

4. The fact that in some instances several cases of this rare disease have occurred in the same family. Hypertrophic biliary cirrhosis not infrequently occurs in several members of the same family, and has been thought by Boix * to be a water-borne disease. Against the view that so-called congenital obliteration of the bile-ducts is in reality a form of congenital cirrhosis it might with reason be objected that the poison that sets up the change must pass through the mother, and that she should show evidence of its influence.

As bearing on toxic processes being conveyed from the mother to the liver of the fœtus through the placental circulation, it is worth referring to the experiments of Nattan-Larrier.† Inoculation of a pregnant guinea-pig with typhoid bacilli

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* Boix: Soc. de biolog., March 12, 1898, p. 297.

† Nattan-Larrier: Soc. de biolog., Nov. 3, 1900.

leads to inflammatory changes in the livers of the offspring. Degenerative changes in the hepatic cells were found by Charrin and Delamare * in the infant of a woman who had eclampsia before its birth.

It is also noteworthy that the extremely fatal biliary cirrhosis in Brahmin infants around Calcutta, which is also a family disease, has been thought to depend on the mother's milk. The mothers restrict themselves to a dry diet and take a decoction of black pepper. If this is the causal factor, it evidently affects the nurslings more than the nurses, and might justify the suggestion that in fœtal life the infant's liver may be more susceptible than the mother to poisons tending to produce cirrhosis; just as the effects of syphilis may be, and usually are, much more manifest in the infant than in the syphilised mother.

To sum up, it seems reasonable to believe that the disease is primarily started by poisons derived from the mother and conveyed to the liver of the fœtus, and that a mixed cirrhosis and cholangitis are thus set up. The cholangitis accounts for the jaundice, and by descending to the larger extra-hepatic bile-ducts, induces an obliterative cholangitis analogous to obliterating appendicitis. In some cases, especially those fatal early in life, the latter change has not been effected, and cirrhosis alone is found. Possibly in some instances this change never occurs, and in this way some of the cases of cirrhosis in very early life are accounted for. Again in exceptional instances the obliterative cholangitis might possibly be delayed and come on much later; such an event might bring Treves' case, already referred to, into line with the others. It is possible that there are several conditions at present included under the title congenital obliteration of the ducts, and that some, such as D. Ross' case, are due to constriction of the duct by localised peritonitis, and deserve the title better than those cases that are intimately associated with cirrhosis.

MORBID ANATOMY.

The liver is, in the great majority of the cases, enlarged, and sometimes to a very considerable extent. In a case published in conjunction with Dr. Hayne (*vide* p. 649) it weighed twice as much as normal. In only one of Thomson's cases was it definitely stated to have been small. The liver is bile-stained, and often dark green; the surface is usually irregular and somewhat resembles ordinary cirrhosis; in only a few cases has the surface been smooth. On section, the organ is tough, firm, and manifestly fibrosed. Cirrhosis is met with in nearly all the recorded cases, but exceptionally it is absent. The lymphatic glands in the portal fissure may be enlarged.

Microscopically there is well-formed fibrous tissue separating the lobules from each other. The arrangement of the fibrous tissue varies: in parts it is monolobular and separates each individual lobule from its fellows (*vide* Fig. 81), in other parts a varying number of lobules are enclosed in firm strands of fibrous tissue. There is thus a mixed cirrhosis composed of the monolobular and multilobular forms. The small bile-ducts often contain plugs of inspissated bile which give the liver as a whole its dark-green colour. In some cases proliferation of the liver cells, giving rise to pseudobile canaliculi, has been seen. The liver cells are in places well preserved, while elsewhere they are in a state of icteric necrosis and do not take the stain.

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* Charrin and Delamare: Compt. Rend. Acad. des Sciences, July 1, 1901, t. cxxxiii, p. 69.

Condition of the Bile-ducts and Gall-bladder.—There is very considerable variation both in the situation and the extent of the obliteration of the ducts. There is a group of cases resembling the present category in clinical features and in the cirrhotic condition of the liver, but without obliteration of the ducts. Now although they cannot, of course, be included in the same class, some of them may with great probability be regarded as an early stage of that condition and may show commencing changes in the ducts, such as thickening.

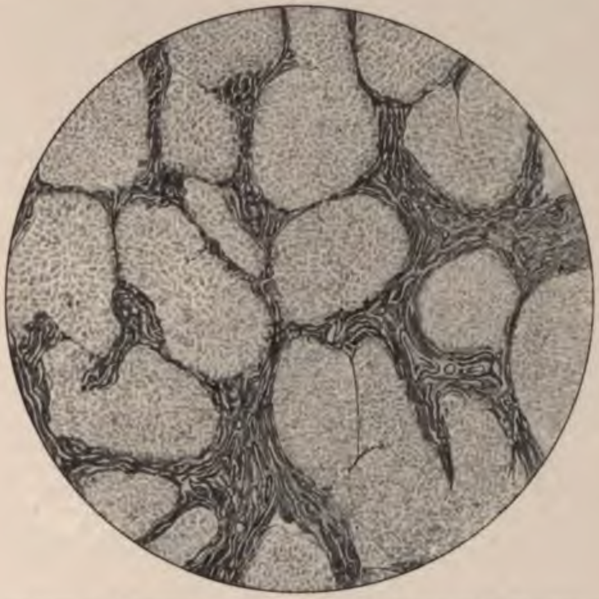

Fig. 81.—Monolobular Cirrhosis from a Case of Congenital Obliteration of the Bile-ducts in a Child Aged Six Months.

There is well-formed fibrous tissue, with no sign of recent proliferation, separating the individual lobules. × 18.

There is no one position in the course of the ducts where obliteration occurs in such a proportion of cases as to justify its being considered the site of election, but it appears to be more frequent towards the lower end of the common bile-duct. The gall-bladder, the cystic, hepatic, or common bile-ducts may each be affected to the exclusion of the others, or there may be widespread obliteration of the biliary tract. The obliterated ducts may be traced in the lesser omentum as fibrous cords which closely resemble the hepatic artery. These fibrous cords may gradually fade off into the surrounding tissues so that the continuity of the obliterated duct cannot be traced any further. In some instances dilatation above the obstruction may occur.

In Oxley's * case of a female infant aged six weeks the common duct, which formed a cyst as large as a cocoanut and contained 36 ounces of bile, was obliterated at the duodenal end.

It is possible that some of the cases of great cystic dilatation of the ducts (*vide* p. 651) are the outcome of partial obliteration of the ducts started in very early life. The gall-bladder may be collapsed and buried in adhesions, or thickened and without any cavity. It may contain some clear mucus, but rarely bile. In one of Thomson's cases a calculus was found in the gall-bladder.

From the extreme paucity of the descriptions of the microscopic appearances of the ducts I am obliged to rely chiefly on my own observations. In my own case the ducts near the point of obliteration showed very considerable fibrous thickening of its walls, with complete alteration of its normal appearance, its muscular tissue and mucous glands having disappeared. The epithelial lining was lost, and the lumen contained débris and masses of bile-pigment which infiltrated the fibrous walls for a short distance. In this case there was, as in the liver, well-formed fibrous tissue and no sign of any progressive hyperplasia or inflammation.

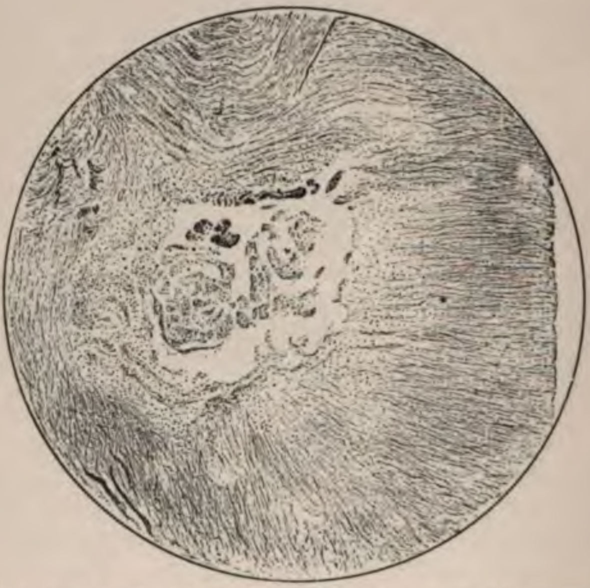

FIG. 82.—TRANSVERSE SECTION OF COMMON BILE-DUCT CLOSE TO ITS OBLITERATION. UNDER A LOW POWER. (× 35.)

Shows altered and fibrosed walls of duct, and absence of mucous glands and of the lining epithelium. The small black spots infiltrating the walls of the duct are microscopic masses of inspissated bile, not nuclei.

In one of Thomson's own cases the gall-bladder, which was partly obliterated, showed thickening of its walls and infiltration with round cells, while, strange to say, the lining epithelium, where any cavity remained, was described as normal.

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* Oxley: Lancet, 1883, vol. ii, 988.

The spleen is enlarged, sometimes very greatly.

In a child aged six months recorded by Parker * the spleen weighed 5 ounces.

The other organs are deeply bile-stained. Adhesions around the liver or bile-ducts are rare, and probably chiefly occur in cases with a syphilitic taint. A small quantity of ascites is recorded in some of the cases, but is of no clinical importance.

CLINICAL PICTURE.

Jaundice may be present at birth or it may succeed on what is regarded as physiological jaundice. In some instances the infant does not develop jaundice until two or more weeks after birth. It is a difficult question whether the effects of congenital changes in the ducts, like those of congenital morbus cordis, may be delayed, and not show themselves until some years have elapsed. If so, cases like Treves' and Ashby's can be explained as really belonging to this category. When once established, the jaundice is progressive and eventually may become dark green, but variations may occur, jaundice becoming less for a time and then darker again.

The urine contains much bile-pigment and stains the napkins. The meconium passed by the infants is usually normal, and is only rarely devoid of bile. In only a few instances have the subsequent motions contained bile. As a rule, normal yellow motions are never passed and the stools are clay-coloured from the first. In some instances, however, a green motion has been described after calomel has been given.

This occurrence has given rise to some discussion; it has been suggested that the green colour may be entirely independent of bile, and due to some chemical combination of mercury and sulphur (Thudichum †), or that the green colour is due to chromogenic micro-organisms. (Lesage.‡) There seems very slender proof that green stools are due to bacterial pigment alone. (Kanthack, Garrod, and Drysdale.§)

It is possible that in the few cases where the administration of calomel has been followed by a green stool there was biliverdin present and that either there was not complete obstruction of the bile-duct or that the administration of calomel set up ulceration of the intestine and so allowed some bile-stained exudation to pass into the bowel.

As might be expected from the absence of bile from the intestine, constipation is the rule, but in a few cases attacks of diarrhœa have been noticed, and may be due to virulent microbic infection of the alimentary canal.

Hæmorrhages from various mucous surfaces into the skin, and from the umbilicus occur in a large number of the cases. Blood may be lost by epistaxis or vomited or passed by the bowel. I have seen fatal hæmoptysis in a case (*vide* p. 649) of this nature. The conjunctivæ, which are deeply stained, may show small hæmorrhages. Bleeding due to constant oozing from the umbilicus may occur soon after birth, and is a very grave symptom, since death follows in a few days. Subcutaneous hæmorrhages may be scattered all over the body like flea-bites.

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* Parker, G.: Lancet, 1901, vol. ii, p. 520.

† Thudichum: Lancet, 1889, vol. i, p. 631.

‡ Lesage: Archives de Phys. Norm. et path., fourth series, 1888, p. 212.

§ Kanthack, Garrod, Drysdale: St. Bartholomew's Hospital Reports, vol. xxxiii, p. 13.

The hæmorrhages, like those seen in other forms of deep obstructive jaundice, in advanced cirrhosis, and in acute atrophy, are due to hepatic insufficiency and the passage of poisons, which should have been stopped by the liver, into the general circulation, and may conceivably be due to diminished coagulability of the blood, to degenerative changes in the vessel walls, or to both these factors. It would be interesting to know whether the coagulation time of the blood in this form of jaundice is prolonged in the same way as it is in other kinds. The liver is enlarged, sometimes so considerably as to reach down to the level of the anterior-superior spine, and is firm, very hard, and fairly smooth. The spleen is also enlarged and firm.

The infants are poorly nourished, and usually become very much wasted if life is sufficiently prolonged, but careful feeding may delay emaciation. Convulsions may come on before death.

Duration and Prognosis.—A certain number of the cases die within the first few days of life from umbilical or other hæmorrhages. Of Thomson's 49 cases, 30 lived more than one month, and of these, 16 survived for upwards of four months, two living into the eighth month. Still * mentions a case examined by him in which death took place at the age of nine and a half months. It is clear that the prognosis is extremely bad. Possibly cases with only slight changes survive for long periods; this is suggested by Treves' case. Moreover, other members of a family in which one child has died of the disease may recover from jaundice in early life.

Tilger † has reported a rather doubtful case bearing on this point. A woman aged forty-six had a gastric diverticulum near the pylorus. This was firmly adherent to the gall-bladder, which was shrunken. The bile-ducts were also abnormal. It was regarded as a congenital affection. Cocking ‡ has reported a case of jaundice in a woman aged fifty which had existed since she was three weeks old. Her liver was large and smooth; the gall-bladder was also enlarged. She had had two children: one died with jaundice at the age of fifteen weeks; the other was healthy. It was thought that she might be the subject of congenital obstruction of the ducts of a slight degree.

DIAGNOSIS.

Deep jaundice, hæmorrhages, with enlargement of the liver and spleen and the absence of any evidence of acute septic infection in a child a few weeks old, point to this disease.

Differential Diagnosis.—Since it is usually manifest that the condition is one of severe jaundice, it is hardly necessary to insist on the distinctions from the slight and common jaundice occurring in the first few days of life, in which the fæces contain bile and the jaundice rapidly fades.

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* Still: Clinical Journal, vol. xvii, p. 324, 1901, March 13.
† Tilger: Virchow's Archiv, Bd. cxxxiii, S. 201, 1893.
‡ Cocking: Quarterly Medical Journ., vol. xi, p. 104, Feb., 1903.

From syphilitic disease of the liver, the absence of any history or signs of the disease and the failure of mercurial treatment should distinguish the disease. According to Still, the liver is much harder on palpation during life in congenital obstruction of the ducts than it is in ordinary cases of syphilis.

From infection of the umbilical vein after birth in which hæmorrhage from the navel also occurs, the disease should be distinguished by its much slower course, by the absence of any sign of umbilical infection, and by the fact that at first there may be little in the way of constitutional disturbance.

TREATMENT.

Treatment is chiefly symptomatic. Small doses of grey powder, fractional doses of calomel, salicylates, or salol may be given to minimise intestinal fermentation; and in the later stages chloride of calcium to prevent hæmorrhage. It is always well to try antisyphilitic treatment on the chance that the disease is of this nature. Very little can be expected from operative measures, and it should be remembered that there is considerable risk of hæmorrhage, owing to the patient's jaundiced condition. Since the obstruction may be in the hepatic ducts, opening the abdomen to do a cholecystenterostomy is a speculative or "exploratory" operation. The only cases in which it is really indicated are those, and they are very rare,—Oxley's, Ashby's, and one of Parker's,—where a cyst is palpable in the abdomen.

Unsuccessful operations have been performed in two cases (Giese and Putnam's), while success followed in Treves' case, referred to on page 640.

Since the disease has a distinct tendency to recur in several members of the family and very probably depends on poisons generated in the mother, it is reasonable to treat the pregnant woman with small doses of calomel ($\frac{1}{40}$ to $\frac{1}{20}$ gr.), salol, and other drugs which tend to inhibit intestinal fermentation, and to pay special attention to her diet and general health during pregnancy.

The following case, which was published by Dr. Hayne and myself, gives a good idea of the disease:

A male child, aged six months, had been jaundiced since birth; it was treated as an out-patient with mercury and chalk, magnesium sulphate, and podophyllin. The jaundice varied from time to time, and the child's nutrition was fairly preserved. A fortnight before death the jaundice became more marked, and on May 28, 1897, the child was admitted. The child then had universal, but not extreme, jaundice. There was some erythema in the left axilla. The liver was much enlarged, and came down to the anterior superior spine of the ilium. The spleen was also enlarged, and projected three fingerbreadths below the costal arch. There was no ascites. The urine was bile-stained, and the motions clay-coloured. On June 5th the temperature went up to 102°, and the child died after bringing up blood from the lungs. The child was the first-born, and presented no signs of congenital syphilis.

The necropsy was performed by Dr. Hayne. The body was thin, and all the organs and tissues were bile-stained. The œsophagus was normal and free from staining by blood. The pleuræ were healthy. The trachea contained blood. Blood was found to have been aspirated into both lungs, which showed emphysematous bullæ and some small caseous masses; the latter were chiefly close to the surface of the lung. Microscopically these caseous areas showed bronchopneumonia, with early caseation, but no definite evidence of tuberculosis. One of the tracheal glands was enlarged and caseous. The liver weighed 12 ounces, or nearly twice the normal weight. (Holt gives 7.5 ounces as the normal weight of the liver for a child of six months, while according to Birch-Hirschfeld 6 ounces is the average weight.) It was much enlarged, yellow in colour, and manifestly cirrhotic. The common bile-duct was small, and as its lower half was transformed into a slender fibrous cord, considerable difficulty was experienced in finding it and in distinguishing it from the hepatic artery. The gall-bladder was small, thickened, collapsed, and buried in adhesions; the cystic duct was represented by a thin fibrous cord. There were enlarged glands in the portal fissure, suggesting the condition found in hypertrophic biliary cirrhosis. The liver cut like a cirrhotic liver and showed fibrosis.

Microscopic sections were taken from various parts of the liver; fibrosis was everywhere present, but the appearances varied in different situations. Where the fibrosis was least marked there was monolobular cirrhosis, the fibrous tissue being old and including a large number of newly formed bile-ducts; in other situations, where the cirrhosis was multilobular, there were areas of extensive fibrosis, including compressed liver cells and small bile-ducts. Some of the latter were dilated and contained plugs of inspissated bile. The cirrhosis was everywhere old and not progressive. The liver cells inside the lobules were in a very fair state of nutrition, the trabecular arrangement was disturbed, and the columns of liver cells were separated from each other by spaces, which, however, appear empty. The appearances are, therefore, those of a mixed monolobular and multilobular cirrhosis. The microscopic appearances of the bile-duct have already been described on page 646.

The spleen weighed 2½ ounces, and was extremely diffluent. The heart, pericardium, kidneys, and other organs were normal, except for bile-staining.

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Hawkins, F. H.: Trans. Path. Soc., vol. xlvi, p. 76.
Kynoch: Edinburgh Med. Journ., July, 1896.
Menzies, G. D.: The Australas. Med. Gaz., Jan. 20, 1904, p. 20.
Parker, G.: Lancet, 1901, vol. ii, p. 520 (3 cases).
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Steven, J. L.: Glasgow Med. Journ., Jan., 1897.
Still, G. F.: Clinical Jour., vol. xvii, p. 324, March 13, 1901.
Wollstein, M.: Archives of Pediatrics, March, 1902.

DILATATION AND CYSTIC TUMORS OF THE BILE-DUCTS.

In obstruction in the course of the common bile-duct backward pressure leads to dilatation of the common and other bile-ducts extending into the liver substance. Whatever the nature of the obstruction, dilatation will occur, but it is, generally speaking, less when due to gall-stone in the common duct than when the obstruction is due to pressure exerted from without by a tumor, such as carcinoma of the pancreas.

Terrier, Mayo Robson,* and Swain† have recorded cases of excessive dilatation of the common duct due to gall-stones.

This depends on the fact that in gall-stones the obstruction is not so complete as in the case of tumors. Exceptionally the dilatation is very excessive and gives rise to a tumor of the common bile-duct containing many pints of fluid.

As a curiosity, Todd's ‡ case may be mentioned. In a girl fourteen years of age the common and hepatic ducts were enormously dilated and contained more than a quart of bile. The cyst reached from the liver to the sacrum and lay behind the duodenum, pancreas, and root of the mesentery. The cause of this dilatation was a "scirrhous state" (chronic interstitial pancreatitis?) of the pancreas.

CYSTIC TUMORS OF THE BILE-DUCTS.

In rare instances great dilatation of the common bile-duct, forming a gigantic cyst, occurs in children. There may be no very evident cause for obstruction, and the condition has been spoken of as idiopathic and has been compared to congenital hydronephrosis (Russell). In some of the cases there may have been partial congenital obliteration of the common duct near its lower end. In Oxley's § case, where the common duct was dilated so as to form a cyst the size of a cocoanut, its duodenal termination was obliterated. It is, however, possible that the cyst gives rise to kinking and obstruction in the distal part of the common duct. In a case recorded by Roslowzew there was a valve-like fold of mucous membrane at the lower end of the common bile-duct. If, as in congenital morbus cordis, changes initiated during fœtal life can remain latent for years and then, possibly as the result of slow cicatricial contraction of inflammatory tissue, give rise to obstruction, a satisfactory explanation is obtained of the following remarkable case recorded by Ashby ‖:

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* Mayo Robson: Diseases of the Gall-bladder, p. 196, ed. iii.

† Swain, W. P.: Lancet, 1895, vol. i.

‡ Todd: Dublin Hosp. Reports, 1817, vol. i, p. 328. Quoted by Legg, Brit. Med. Journ., 1874, vol. i, p. 607.

§ Oxley: Lancet, 1883, vol. ii, p. 988.

‖ Ashby: Medical Chronicle, Oct., 1898, p. 28.

A girl aged seven had been jaundiced for two and one-half years, and more recently had been tapped to the extent of 50 ounces for ascites. She was emaciated and had œdema of the feet. A cyst on the right side of the abdomen was tapped and 16 pints of dark-green mucus came away. In the course of three months it was tapped ten times, and on each occasion 8 to 10 pints were removed. After death the cyst was found to be the dilated common bile and cystic ducts; no communication with the duodenum could be made out.

Possibly in the following case obstruction in the common duct was due to hereditary syphilis:

In the case of a deeply jaundiced child aged nine years there was very marked evidence of hereditary syphilis in the body generally, and in the liver in pericellular cirrhosis. The liver and biliary apparatus preserved in the Museum of the College of Medicine, Newcastle-on-Tyne (No. 382–2), show the common bile-duct dilated to the size of one's fist, the cystic and hepatic ducts being also dilated, while the gall-bladder is atrophied and collapsed and the opening of the common bile-duct into the duodenum cannot be found. There was, however, no convincing proof that the obstruction of the bile-duct was due to any syphilitic process, such as ulceration and cicatrization.

In some of the recorded cases the cysts have been extraordinarily large, and when first seen on opening the abdomen, have resembled ovarian or hydatid cysts. The fluid inside them contains bile-pigments. In Wilks and Moxon's case,* referred to elsewhere (*vide* p. 681), the common bile-duct of a child aged four years, which was dilated so as to be as big as its head, contained a number of pendulous growths.

According to Roslowzew,† this condition has only been met with in females. The following case in a boy, however, has been recorded by Russell:

A boy aged eight years had jaundice, fever, and a large elastic tumor reaching from the liver to the iliac crest and middle line. It was thought to be catarrhal jaundice, which was prevalent in Melbourne at the time, in a child the subject of a hydatid cyst. The cyst was found to be the dilated common, hepatic, and cystic ducts. It contained some small bilirubin-calcium calculi. The opening into the duodenum was small and valvular.‡

Clinically these cases present themselves as abdominal cysts in connexion with the liver and may be regarded as ovarian or hydatid cysts. Jaundice is present. The **prognosis** and **treatment** are not very satisfactory, as judged by the results of the recorded cases. Probably drainage of the cyst and exploration of the lower end of the common bile-duct with a probe so as to displace any valvular fold of mucous membrane and allow a free passage of bile into the duodenum are the best means at our disposal.

Bile-containing Cyst in Communication with the Ampulla of Vater.—As a pathological curiosity a brief description may be given of a specimen, dissected by Dr. R. S. Trevor, of a cyst containing bile, the size of a tangarine orange, which projected into the duodenum in the situation of the biliary papilla. It was lined inside and out by mucous membrane and its only communication was with the cavity of the ampulla of Vater. It appeared to be a sacculus of the ampulla and to be comparable with a sacculus of the urinary bladder; the mucous membrane lining it being that of the ampulla and the mucous membrane on its outer surface that of the duodenum. It was found in the body of a man, aged twenty-four years, who died in St. George's Hospital from a perforated duodenal ulcer. There was no jaundice and no gall-stone.

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* Wilks and Moxon: Pathology, p. 485, 3d ed., 1889.

† Roslowzew: Deutsche med. Wochen., Bd. xxviii, S. 739, 1902.

‡ Russell: Annals of Surgery, Dec., 1897, p. 692.

SIMPLE STRICTURE OF THE BILE-DUCTS.

With the exception of the cystic duct, this is a very rare condition. The cases may be divided into two distinct groups: (i) the congenital cases, described on page 639 in the section on Congenital Obliteration of the Bile-ducts, and (ii) those acquired in later life, which will be dealt with here. It is possible, though it is a speculative point, that in some of these cases also a congenital factor may be present. A slight congenital change in the ducts might gradually progress so that it would only give rise to bad effects some years after birth. This point is referred to in the account of congenital obliteration of the ducts.

Incidence.—It is generally assumed that ulceration of the common ducts due to gall-stones may, by cicatricial contraction, lead to stenosis, but this sequence is surprisingly rare.

Pye-Smith [*] has recorded a case, and a good example of a tight stricture of the common duct with a soft calculus just above it, in a woman aged twenty-six, is described in St. Thomas' Hospital Reports.[†] In cases of simple stricture recorded by Holmes [‡] and Moxon [§] the stricture was at the commencement of the common hepatic duct and therefore not much exposed to calculi, except small bilirubin-calcium calculi. In Moxon's and Phillips' [‖] cases there was no history of cholelithiasis.

In the following case the termination of the common bile-duct was obliterated, apparently as the result of cicatrisation of an ulcer due to gall-stones:

> A woman aged forty-six years was operated upon for recurrent attacks of biliary colic. The gall-bladder was empty and contracted, but the cystic duct was dilated by five calculi, which were removed. The cystic duct was united to the abdominal wound, and bile was discharged for ten days. The patient then got worse and died suddenly. At the autopsy the common bile-duct was dilated and contained several calculi; its opening into the duodenum was completely obliterated by cicatrisation of an ulcer.[**]

Stricture and obliteration of the cystic duct in cholelithiasis and cholecystitis are comparatively common, and thus form a marked contrast to the other large bile-ducts.

It is conceivable that in some cases simple stricture is due to ulceration occurring in the ducts as the result of cholangitis set up by typhoid or influenzal infection. Possibly syphilitic inflammation may account for some of the cases. Lazarus-Barlow * has recorded a case of stricture occurring in a boy the subject of hereditary syphilis, but in this instance and in that described by H. Mackenzie † the cicatricial process probably started outside the ducts and compressed them from without. (*Vide* p. 543.)

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[*] Pye-Smith, P. H.: Trans. Path. Soc., vol. xxiv, p. 250.

[†] St. Thomas' Hospital Reports, vol. xxix, p. 169.

[‡] Holmes, T.: Trans. Path. Soc., vol. ix, p. 130.

[§] Moxon, W.: Trans. Path. Soc., vol. xxiv, p. 129.

[‖] Phillips, S.: Trans. Clinic. Soc., vol. xxi, p 26.

[**] St. Bartholomew's Hospital Reports, vol. xxxv. Surgical Registrar's Reports, p. 216.

The following is the only case of simple stricture of the common bile-duct which has been detected at St. George's Hospital in the last fifteen years:

A man aged sixty years, with chronic jaundice, was admitted with pneumonia which proved fatal. There were a fibrous stricture of the common bile-duct in its lower fourth and great distension of the gall-bladder and bile-ducts. There was no evidence of any malignant disease or of gall-stones.

It should be remembered that some of the cases of stricture of the bile-ducts in adults may, in the absence of microscopic examination, have been cases of primary carcinoma of the ducts, as a stricture which, to the naked eye, appears merely fibrous, may be undoubtedly carcinomatous.

This was the case in a woman aged fifty-seven in whom the lower part of the common bile-duct was much stenosed as if from cicatrisation of an ulcer due to gall-stones. Microscopically it was carcinomatous.‡

The **symptoms** are those of chronic obstructive jaundice and resemble those of malignant disease of the bile-ducts. In Moxon's case, where jaundice lasted eight months, there was much xanthelasma on the hands, back, and scrotum.

An accurate diagnosis is impossible before the abdomen is opened and the duct freely exposed.

Treatment.—If there is a suspicion of syphilis, iodides should be given. Failing any improvement from antisyphilitic treatment, an exploratory operation with a view of uniting the gall-bladder with the intestine, if the stricture is in the common bile-duct, should be undertaken.

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* Lazarus-Barlow, W. S.: Trans. Path. Soc., vol. l, p. 158.

† Mackenzie, H.: Trans. Path. Soc., vol. xlvii, p. 84.

‡ Krokiewicz: Wien. klin. Wochen., March 31, 1898, S. 321.

SIMPLE CATARRHAL JAUNDICE OR ACUTE CATARRHAL CHOLANGITIS.

Definition.—Local inflammatory swelling of the mucous membrane of the termination of the common bile-duct leading to biliary obstruction and to the passage of bile into the circulation. The jaundice is preceded by signs of gastro-intestinal catarrh, comes on without pain, and lasts about three weeks.

It is essentially due to a local inflammatory obstruction, and must be distinguished from toxæmic and infectious jaundice (Weil's disease), which are the manifestations of a general toxæmia or hæmic infection. Catarrhal jaundice is due to acute catarrhal inflammation limited to the biliary papilla and the adjacent portion of the common bile-duct, and but for the objection to coining new terms, might be spoken of as acute cholo-papillitis.

While adopting this view as to the nature of acute catarrhal jaundice, it is well to admit that there is room for discussion as to the part played by infection and inflammation spreading from the duodenum. Gastro-duodenal catarrh may be toxic or due to microbic activity, and in the latter case the jaundice might be spoken of as being infective. The French school,* indeed, includes catarrhal jaundice among the benign or innocent forms of infective jaundice. Besides mechanically obstructing the lower end of the bile-duct, the morbid process may extend upwards and involve a greater or lesser extent of the common bile-duct. When a considerable extent of the common bile-duct is inflamed, the condition usually becomes one of chronic cholangitis and clinically presents itself as one of prolonged catarrhal jaundice.

CAUSATION.

Gastroduodenal catarrh involving the mucous membrane of the biliary papilla readily spreads into the common channel, or ampulla of Vater, inside the biliary papilla. Comparatively little swelling of the mucous membrane of the narrow orifice of the papilla is sufficient to obstruct the flow of bile through it, while a plug of tenacious mucus may easily form in the lumen of the papilla. Probably this is what happens in the ordinary run of cases, though it is not improbable that inflammatory swelling spreads a varying distance up the common bile-duct in more prolonged examples of the disease. Some cases, which apparently begin as catarrhal jaundice, rapidly develop into acute yellow atrophy, and it is possible that an inflammation of the lower end of the common duct has rapidly extended up to the liver.

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* Chauffard: Traité de Médecine (Bouchard, Brissaud), tome v, p. 89, 1902.

The causes of catarrhal jaundice are, therefore, those of gastroduodenal catarrh; it is a complication of acute gastritis and may be due to alcoholic excess or indiscretions in diet, and follows chills.

Since gastritis is a very common accompaniment of the specific fevers, it is easy to understand that jaundice in the course of typhoid fever or pneumonia may depend on purely local obstruction at or near the biliary papilla. On the other hand, it must be remembered that when seen in the course of the specific fevers, jaundice may be toxæmic, or depend on severe infective inflammation of the bile-ducts and gall-bladder.

In typhoid fever jaundice is remarkably rare—so much so that Sir W. Jenner * never met with it. When it does occur, it may be catarrhal, toxic, or the expression of infection of the biliary passages leading to cholangitis, etc. When catarrhal jaundice occurs in typhoid fever, it may be met with at any period in the course of the fever or in a relapse, and in no way affects the course of the disease.

Osler † records 6 cases, 2 in relapses; 5 of these occurred in 829 cases of typhoid fever at Johns Hopkins Hospital. Da Costa,‡ in a review of 52 cases of jaundice in the course of typhoid fever, found 4 due to catarrhal jaundice. In 244 cases of typhoid, which I analysed, at the Imperial Yeomanry Hospital, Pretoria, there was one case of mild catarrhal jaundice.§ I have seen similar cases in England.

Catarrhal jaundice may supervene in the course of portal cirrhosis and be due to gastroduodenal catarrh, which, of course, is favoured by chronic portal engorgement and may be lighted up by alcoholic excess. A slight icteric tinge of the skin is very frequent in advanced cases of mitral disease; it is only exceptionally that there is intense jaundice. It may also occur and be perhaps the first symptom in cases of malignant disease involving the liver or bile-ducts.

Thus in two cases under my care in St. George's Hospital at the same time in 1897 jaundice came on suddenly with vomiting and signs of gastro-enteritis: one was a woman with primary carcinoma of the gall-bladder; the other, a man with primary carcinoma of the common bile-duct. In both cases the jaundice lasted until death.

Catarrhal jaundice may also complicate other organic diseases of the liver, such as hydatid. Emotional jaundice has been thought to be really catarrhal in origin, but without sufficient grounds. Catarrhal jaundice may be epidemic because gastroduodenal catarrh is epidemic. It must, however, be borne in mind that epidemic jaundice is usually toxæmic and due to descending infection of the small intra-hepatic ducts set up by some microbic infection or toxine. As examples of this epidemic infective jaundice, Weil's disease (*vide* p. 584) and jaundice following drain poisoning may be mentioned. It is not always easy to be dogmatic as to the nature of mild epidemic jaundice; probably most cases are toxæmic rather than purely local catarrh of the lower end of the common bile-duct. It is, however, probable that mild epidemic jaundice following influenza may belong to the latter category.

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* Jenner, W.: On Fevers and Diphtheria, p. 353.

† Osler, W.: Johns Hopkins Hosp. Reports, vol. viii, p. 372, 1900.

‡ Da Costa: American Journ. Med. Sciences, July, 1898, vol. cxvi, p. 1.

§ Rolleston: Brit. Med. Journ., 1901, vol. ii, p. 976.

MORBID ANATOMY.

Opportunities for investigating the morbid conditions underlying catarrhal jaundice only arise when death occurs from some other cause, such as an accident.

The mucous membrane of the duodenum and adjacent part of the common bile-duct is swollen, injected, and covered by tenacious mucus. A plug of inspissated mucus may be found inside the termination of the common bile-duct. These changes rarely extend further up than the lower end of the common bile-duct.

The swelling of the mucous membrane may, however, subside after death, and because it is possible to force bile into the duodenum by pressure on the gall-bladder it does not follow that there was no obstruction during life. The same remark applies, only with more force, to the passage of a probe up the bile-duct from the duodenum. The liver may be swollen from accumulation of bile and from vascular engorgement. The lining membrane of the heart and vessels is bile-stained.

CLINICAL PICTURE.

Incidence.—In an analysis of 215 cases of simple catarrhal jaundice Neumann * found that 42 per cent. occurred in the first ten years of life, and here it may be mentioned that sucklings appear to be rarely affected by this particular form of jaundice; between ten and twenty years 10 per cent. of the cases occurred, while the percentage rose to 27 per cent. in the third decade. It is commoner in the winter than in the summer months.

Premonitory Symptoms.—Before jaundice appears there are usually, though not invariably, signs of gastro-intestinal disturbance which may last for a few days to a week. There are vomiting, loss of appetite, furred tongue, foul breath, bitter taste in the mouth, headache, vertigo, and dyspepsia, some general malaise, and occasionally flying pains in the limbs. Diarrhœa from extension of the catarrh to the intestines is often seen. The motions become clay-coloured and free from bile-pigment before the appearance of icterus and markedly offensive from fermentation. The fæces may remain pale for a considerable time; this need not always be due to the absence of bile, but may depend on milk taken as food, and on the fæces containing gas in a finely divided state. Jaundice may not be noticed by the patient until his attention is directed to it by his friends.

The conjunctiva is the first part of the body to show the icteric tint, but the presence of bile-pigment can be detected in the urine even before this. The sclerotics under the conjunctivæ are one of the most suitable sites for recognising the jaundice, but the fatty and often slightly yellow masses (pingueculæ) underneath the conjunctivæ must not be mistaken for icteric tingeing.

The skin of the face becomes jaundiced soon after the conjunctivæ. This is more manifest in blonds than in dark-skinned persons, who are often naturally somewhat sallow. The mucous membrane of the mouth, especially under the tongue and on the inner surface of the lips, appears yellow when the blood is pressed out of the superficial vessels. From the face the yellow tint spreads to the trunk and extremities, reaching the legs last; the whole of the body finally becomes jaundiced, and sometimes of a bright yellow colour. The dark green colour seen in obstructive jaundice due to malignant disease is never seen in catarrhal icterus; but the skin may show the effects of jaundice for a considerable time.

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* Neumann: Deutsche med. Wochen., Aug. 31 1899.

Osler * mentions a case in which stigmata or spider angiomata appeared on the face during catarrhal jaundice.

By the time that jaundice has made its appearance the gastric symptoms have usually begun to subside. This, however, is by no means universal. Obstinate vomiting may persist when the diet is not carefully restricted and supervised. At the onset there may be slight fever from the gastro-enteritis, but otherwise the temperature is either normal or considerably below the normal. It is often stated that there may be fever in catarrhal jaundice. It is probable that cases which otherwise resemble catarrhal jaundice but show a raised temperature are rather to be classed as mild cases of toxæmic or infective jaundice.

Symptoms when the Disease is Fully Developed.—The pulse is slowed; this is usually referred to the action of bile salts on the cardiac ganglia. It is often 60 or less per minute, and is of low tension, soft, and may be dicrotic. The slowing of the heart's action is much less marked in children than in adults. Pruritus is often a troublesome feature; the scratching may lead to traumatic eczema, or even to an urticarial rash. Pruritus is rare in children, as shown by the fact that Still † has never met with an example. It is by no means certain how the itching is brought about; it may be absent when jaundice is very marked, and may appear before any icterus is perceptible; so it cannot be very satisfactorily explained by the action of the bile on the cutaneous nerves. Yellow vision (xanthopsia) is sometimes, though rarely, present; its existence is seldom a cause of complaint, but the patients may be found to have noticed it on being questioned. It is thought to be due to bile in the vitreous humour. Owing to the action of the bile constituents in the brain there are depression of spirits and, sometimes, a melancholic condition. There may be much mental irritability and incapacity for transacting the ordinary affairs of life efficiently.

The urine contains bile-pigment On shaking it in a white porringer the foam becomes characteristically yellow. During the first few days and even before jaundice has appeared on the surface of the body bile acids as well as bile-pigment may be present in the urine. During the period of the disease when the patient feels worst there may be a distinct excess of nitrogen in the urine as compared with that taken in. During this time the patient loses weight.‡ While there is bile in the urine casts may be found, but not albumin.

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* Osler: Johns Hopkins Hosp. Bull., vol. xii, p. 337, 1901.

† Still, G. F.: Clinical Jour., vol. xvii, p. 324, March 13, 1901.

‡ Schmidt: Centralbl. f. innere Med., Feb. 5, 1898

The occurrence of bile-pigment in the saliva in cases of jaundice has been recorded by various authors, especially when, as a result of mercurial treatment, inflammatory changes in the mouth are superadded. W. Legg,* who paid special attention to this point, always found the saliva colourless in cases of uncomplicated jaundice. The sweat, especially from the armpits, may contain bile-pigment, and the linen may be stained, but, generally speaking, the perspiration is colourless. The secretion of the alimentary canal, the tears, nasal mucus, and in women the milk, are, in spite of statements to the contrary, free from bile. In inflammatory conditions the altered secretions and exudations become bile-stained; this is shown in pneumonic sputum and in pleural and peritoneal effusions.

The blood-serum contains bile-pigment, but there is no change in the corpuscles. As has been pointed out above (p. 535), the serum of jaundiced patients has been said to agglutinate typhoid bacilli. Dr. H. Spitta has kindly given me the notes of the agglutination reactions in eight cases of catarrhal jaundice. In two cases there was slight clumping of typhoid bacilli in a dilution of 1 : 10; in none of the cases was there any clumping of Gärtner's bacillus. Bacillus coli was agglutinated in all the cases in dilution of 1 : 10, and in six of the cases in a dilution of 1 : 100.

As a rule, there is no hepatic enlargement or tenderness on palpation. Many authors state that the liver may be enlarged in simple catarrhal jaundice as the result of distension of the intra-hepatic ducts with bile, but if the enlargement is at all marked, it is probable, though it is impossible to speak with any certainty on this point, that inflammation of the common bile-duct has spread to the ducts in the liver substance.

The gall-bladder is sometimes palpably enlarged in cases of catarrhal jaundice, but definite enlargement should always raise the question whether the disease is not in reality cholecystitis with some inflammation of the common bile-duct.

Duration.—The jaundice gradually fades in the course of four to six weeks, but the skin often remains tinged for a considerable period. In slight attacks the icteric tint may pass away in a couple of weeks. Occasionally cases, which begin like ordinary catarrhal jaundice and eventually clear up, hang fire and last for months; Chauffard † quotes cases lasting from ninety-two to one hundred and fifty-five days. These cases are very probably examples of chronic catarrhal cholangitis, and are allied to the chronic inflammation of the common bile-duct set up by calculi (*vide* p. 750), as is shown by the fact that intermissions may occur. Thus, though beginning like catarrhal jaundice, these cases must be regarded as complicated by an extension of the inflammatory process and as belonging to another category. If, in a case regarded as catarrhal jaundice, the disease does not clear up, there is either some complication or the diagnosis is wrong. Relapses of catarrhal jaundice may occur.

Effects.—Considerable loss of flesh and weight occur in a well-marked case of catarrhal jaundice. The loss of appetite and the resulting deficiency in the intake of food largely accounts for this, but the diminished absorption of fats must also be considered as an important factor, since it obliges the patient to live on his own tissues.

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* Legg, W.: St. Bartholomew's Hospital Reports, vol. xiii, p. 12.

† Chauffard: Traité de Méd. (Bouchard, Brissaud), tome v, p. 97, 1902.

Calculi and biliary colic may follow ordinary catarrhal jaundice, but in order to explain cholelithiasis as a sequel of ordinary catarrhal jaundice it must be assumed that the gall-bladder was involved and that cholecystitis of a mild degree was present in addition. Cholelithiasis might thus be a result of a complication of catarrhal jaundice and subsequently give rise to biliary colic. Dilatation of the lower end of the common bile-duct has been thought to be a result of catarrhal inflammation, but it is probable that when this sequence is noted, the inflammation has been of considerable duration or intensity, or that there has been a gall-stone there. Just as the inflammation of the papilla may spread into the common bile-duct and give rise to chronic cholangitis, so the catarrhal process may extend into Wirsung's duct of the pancreas and set up acute or chronic pancreatitis, which may therefore be regarded as possible complications or sequelæ of catarrhal jaundice.

DIAGNOSIS.

The presence of gastro-intestinal disturbance, vomiting, diarrhœa, loss of appetite, and dyspepsia before the onset of jaundice, the absence of severe constitutional disturbance and of pain, and the comparatively mild jaundice fading within a few weeks are the important points in the diagnosis. In some instances gastro-intestinal symptoms are absent and it is then difficult to eliminate at once more serious forms ρf jaundice; it must also be remembered that catarrhal jaundice may complicate grave forms of hepatic disease. The age of the patient has some bearing, as catarrhal jaundice in late middle life may be the first indication of malignant disease involving the ducts. The duration and character of the jaundice are very important; when jaundice lasts more than six weeks, the diagnosis of simple catarrhal jaundice should be seriously questioned, and some other cause sought for. Deep green or "black" jaundice excludes simple catarrhal jaundice. Constantly recurrent attacks point to intermittent hepatic fever and the presence of a calculus in the lower end of the common duct.

Cases of mild toxæmic jaundice are readily confused, especially those with only slight fever and enlargement of the liver, with catarrhal jaundice. In well-defined toxæmic or infective jaundice there are signs of general nfection, such as fever, albuminuria, splenic and hepatic enlargement, but in the milder cases some of these manifestations may be absent and there is a transition to catarrhal jaundice.

From gall-stone colic the condition is distinguished by the gradual and painless onset of jaundice and by preceding gastro-intestinal irritation.

The jaundice accompanying the presence of gall-stones in the common duct is much more prolonged than in catarrhal jaundice, and is usually characterised by periodic outbursts of fever, pain, and exacerbations in the degree of jaundice (*vide* p. 750). It may be preceded by biliary colic, but this is by no means always the case, and it may come on quite gradually. It occurs in older persons than catarrhal jaundice, especially in women.

PROGNOSIS.

In ordinary cases the prognosis is extremely good, there being no danger to life and very seldom any after-results of importance. On the other hand, it must be borne in mind that what at first appears to be catarrhal jaundice may be the initial manifestation of severe organic disease of the liver, such as malignant disease or acute yellow atrophy. It is, therefore, advisable to avoid giving a dogmatic prognosis in the early stages, if this can be done without creating alarm. In the vast majority the result of the case justifies a prognosis of complete and rapid recovery, given at the very outset; but in rare instances the clinical picture radically changes and nervous symptoms rapidly usher in coma and death from acute yellow atrophy, or, in less exceptional cases, the jaundice, instead of gradually disappearing, deepens into that of malignant obstruction of the common bile-duct. When catarrhal jaundice is prolonged, the prognosis alters, as the possibility of some grave cause of obstruction must be considered, but some of these protracted cases recover without any definite developments.

TREATMENT.

In the early stage, while there is evidence of gastro-intestinal catarrh, the patient should be kept warm in bed and on a milk diet. As absorption of fat is greatly diminished, skimmed milk containing one per cent. of fat is preferable to ordinary milk. In the presence of nausea and complete loss of appetite it is unnecessary to press even milk, and for a few days the patient should be allowed to take or leave it; thirst is usually present, and water, lemonade, Apollinaris, Vichy, or Vals water should be provided. The gastric irritation may be allayed by draughts of warm water containing bicarbonate of soda, and by the application of poultices to the upper part of the abdomen. Nausea and vomiting are readily excited by food, and rest to the stomach by temporary starvation is followed by improvement and is well borne. Bismuth in the form of a lozenge or in a mixture with bicarbonate of soda and dilute hydrocyanic acid may also be given.

The bowels should be kept open either by enemata or by a small dose of calomel ($\frac{1}{2}$–1 gr.) given at night and followed next morning by Carlsbad salts. Vigourous purgatives may set up or increase gastro-intestinal catarrh and should, therefore, be avoided.

When the gastro-intestinal catarrh has subsided, the bland milk diet should be relaxed, and clear thin soup, eggs, fish, and white meat given as the patient's condition allows. Minute doses ($\frac{1}{40}$–$\frac{1}{20}$ gr.) of calomel, salicylate of bismuth, and salol are useful to inhibit intestinal fermentation; while β-naphthol, benzo-naphthol, resorcin, and iodoform have been employed with the same object. The action of the bowels must be maintained by the purgative waters or by salines, such as Epsom or Carlsbad salts, phosphate of soda, and, if necessary, by blue pill.

Rectal injections of cold water to stimulate peristaltic action of the gall-bladder and so induce flushing of the bile-ducts by the bile have been recommended. Massage to the liver has been advocated by Gilbert and Lereboullet,* and can be carried out at a spa by the liver douche.

During convalescence a tonic containing dilute nitrohydrochloric acid and nux vomica is useful in improving the appetite and digestion.

For the pruritus, alkaline baths or sponging with carbolic acid lotion, 1 : 40, often give relief, while the internal administration of chloride of calcium in 20-grain doses, or antipyrin, which acts as a nerve sedative, should be tried.

If the jaundice persists and there is no reason to suspect any grave underlying condition, such as malignant disease, the patient will probably receive benefit from a visit to a spa, such as Harrogate, Leamington Llandrindod Wells, Vichy, Neuenahr, Carlsbad, or Bertrich.

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* Gilbert et Lereboullet: Gaz. hebdomin. 1901. p. 913.

SUPPURATIVE CHOLANGITIS.

ETIOLOGY.

The exciting cause of suppurative inflammation of the bile-ducts is a virulent microbic infection; the varieties of bacteria which have been found to give rise to this affection are referred to below (*vide* p. 665). The conditions and diseases which dispose to suppurative cholangitis are—(i) Local; and (ii) general.

(i) **The local conditions** are:

(*a*) Those which diminish the resistance of the ducts, such as new-growth, past inflammation, etc., and (*b*) render infection more easy, such as biliary stagnation, gall-stones, rupture of hydatid cysts into the ducts, the presence of worms in the ducts, etc. Biliary obstruction and stagnation prevent the ducts being flushed out. Hence micro-organisms which have got into the ducts either from the liver and general circulation (descending infection) or from the duodenum (ascending infection) have a better chance of multiplying and setting up inflammatory changes in the ducts, especially since, owing to dilatation, the ducts are probably less resistant than in health.

Cholelithiasis is the commonest antecedent of suppurative cholangitis; this was so in 18 out of 20 cases collected by L. Rogers.* The acute suppurative inflammation may supervene on old-standing infective cholangitis (*vide* Intermittent Hepatic Fever, p. 750) or may occur in a patient who has never had any manifest signs of cholelithiasis. When suppurative cholangitis supervenes on chronic catarrhal inflammation of the ducts, the more virulent microbic infection may be supposed to be favoured by the diminished resistance of the ducts.

Rupture of hydatid cysts into the bile-ducts, though not nearly so frequent a cause of suppurative cholangitis as gall-stones, is a well-established factor. Possibly in the first instances the hydatid fluid may produce a change in the mucous membrane of the ducts, analogous to urticaria. The presence of hydatid membranes in the ducts favours ascending infection from the duodenum, and it is probably to this that suppurative cholangitis is due. The subject of rupture of hydatid cysts into the bile-ducts is considered more fully in the section on "Hydatid Disease of the Liver."

In hepatic abscess the inflammation may spread to the bile-ducts, or the abscess may open into the larger bile-ducts. Cholangitis may thus be secondary to hepatic abscess, and by giving rise to multiple foci of suppuration, renders a fatal issue almost certain.

Round worms and liver flukes may pass up the common bile-duct from the duodenum and carry with them micro-organisms. The ducts thus become infected, and suppuration, either diffuse or localised, of the ducts will readily result. When localised, the worm may be found in an abscess cavity in the liver. (*Vide* Parasitic Affections and Bile-ducts, p. 676.)

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* Rogers, L.: Brit. Med. Jour., 1903, vol. ii, p. 706.

A new-growth—papilloma or carcinoma—arising on the duodenal surface of the biliary papilla is not common, but is very prone to set up suppurative cholangitis. The tendency to the development of suppurative inflammation of the bile-ducts in carcinoma of the duodenal surface of the biliary papilla depends on the following factors: (1) Obstruction to the outflow of bile and dilatation of the ducts diminish their resistance. Owing to ulceration and necrosis of the growth, the obstruction may intermit, and this intermission very probably favours an ascending infection from the duodenum. (2) The presence of the growth favours duodenal catarrh and thus renders ascending infection of the common bile-duct easy. (3) Stagnation of bile in the ducts favours microbic infection.

The growth in the duodenum in the region of the papilla may be either a papilloma or a carcinoma; in some instances it appears to the naked eye to be a papilloma, but microscopic examination shows invasion of the duodenal wall and therefore malignancy, as in the specimens in the Museums of Guy's and St. Bartholomew's Hospitals.

Besides malignant disease of the duodenum, carcinoma of the diverticulum of Vater and of the lower part of the common bile-duct may also lead to suppurative cholangitis. (*Vide* p. 692.)

In malignant disease of the liver pressure on the ducts disposes to and may lead to suppurative cholangitis.

A woman aged forty-four years in St. George's Hospital under the care of my colleague, Sir I. Owen, with jaundice, was operated upon and found to have multiple growths on the surface of the liver. She had a febrile temperature until her death, one week later. The postmortem revealed primary carcinoma of the splenic flexure, which, however, had not given rise to any symptoms, and secondary growth in the liver and in the portal fissure. The latter compressed the hepatic ducts. The intra-hepatic bile-ducts showed suppurative cholangitis. The gall-bladder was collapsed, showed a secondary growth in its wall, but was not inflamed or occupied by any gall-stones.

In rare instances an aneurysm of the hepatic artery may lead to multiple abscesses in the liver. Osler and Ross * have recorded a case. The abscesses may be due to infective emboli, but they may also be the abscesses of suppurative cholangitis. As bearing on the occurrence of suppurative inflammation of the ducts in association with aneurysm of the hepatic artery, it is interesting to note that Dujarier and Castaigne † have found that experimental ligature of the hepatic artery leads to stagnation of bile in the ducts and so favours infection.

(ii) **The General Diseases which Dispose to Suppurative Cholangitis.**—Suppurative cholangitis may occur after infective diseases attacking either the body generally or the alimentary canal.

General blood infections or intoxications may set up inflammation of the small ducts in the liver in the same way that toluylendiamin, when employed experimentally, gives rise to a descending cholangitis. Micro-organisms or poisons may reach the liver by the blood stream, and if the bile-ducts are previously damaged, micro-organisms may gain an entrance into the ducts and so set up cholangitis.

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* Osler and Ross: Canadian Med. Journ., vol. vi.

† Dujarier and Castaigne: Bull. Soc. Anat. Paris, 1899, p. 329

Influenza and pneumonia have in rare instances been precursors of suppurative cholangitis. In both these diseases it is possible that the cholangitis might be an extension of inflammation from the duodenum, since there is a well-known gastro-intestinal form of influenza, and, in rare instances, pneumococcal gastritis.

Suppurative cholangitis after influenza has been recorded by Mayo Robson * and Remy †; in the latter case, cultivations showed the presence of a colon bacillus.

The diseases of the alimentary canal that may be followed by suppurative inflammation of the bile-ducts are typhoid fever and cholera.‡

A great deal has been written about the typhoid affections of the biliary system. Usually the gall-bladder bears the brunt of the disease. It is very rare for suppurative cholangitis to occur independently of cholecystitis, though the two are often combined. In fact, typhoidal suppurative cholangitis is practically subordinate to the concomitant affection of the gall-bladder. Experimentally cholangitis has been set up by the injection of cultures of the comma bacillus into the bile-ducts of rabbits. (Gilbert and Dominici.§)

Bacteriology of Suppurative Cholangitis.—A large number of micro-organisms have been found by different observers to be associated with suppurative cholangitis. In some of the cases where the colon bacillus has grown in the cultures it is not unlikely that other micro-organisms were present, but were crowded out by the vigourous growth of the colon bacillus, and that either a mixed infection was present or that subsequent contamination with the colon bacillus occurred.

The chief organisms found are streptococci, staphylococci (albus, aureus), pneumococcus, typhoid bacillus, comma bacillus, and colon bacillus.

The comma, typhoid, and coli bacilli being motile, ascend the ducts from the intestine more readily than the non-motile streptococci and staphylococci.

The Bacillus aërogenes capsulatus, which usually invades the tissues during the death agony, may, however, be present during life in the circulation and may even be a primary infection.

In a case of multiple abscesses of the liver in carcinoma of the lower end of the common bile-duct a pure culture of Bacillus aërogenes capsulatus was obtained by Pratt and Fulton.‖

MORBID ANATOMY.

The mucous membrane of the ducts is swollen from inflammatory exudation and irregular from ulceration. The outer walls of the duct are also thickened and inflamed, and by extension there may be local peritonitis, which may lead to obliteration of the foramen of Winslow, or, by extension to the portal vein, to pylephlebitis. The glands in the portal fissure are enlarged and soft. What part the lymphatic vessels play in the upward spread of the inflammatory process into the liver it is hard to say, inasmuch as any process of this kind would be against the lymph stream. Possibly some of the areas of suppuration in the liver may arise, as pericholangitic abscesses in connexion with the lymphatics. The suppurative process in the ducts may be associated with an empyema of the gall-bladder.

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* Mayo Robson: Allbutt's System of Medicine, vol. iv, p. 251.

† Remy: Congrès de chirurg., 1896, p. 485.

‡ Galliard: La Cholera, Bibliothèque Charcot-Debove, 1894.

§ Gilbert and Dominici: Mem. Soc. de biolog., 1894, p. 11.

‖ Pratt and Fulton: Boston Medical and Surgical Journ., June 7, 1900, p. 599.

When the inflammation has spread to the liver, that organ is nearly always greatly enlarged, swollen, and of a greyish colour, with yellowish-green areas around the portal spaces. These foci are softening down into suppuration. In early stages these areas may, to the naked eye, resemble secondary nodules of new-growths or even the rarer condition of lymphadenoma. When the disease is fully developed, the bile-ducts may be enormously dilated so as to be as large as the small intestine, or to be opened during laparotomy under the idea that the case is one of suppurative cholecystitis. (Rogers.*)

The dilated and suppurating ducts may terminate in small abscesses on the surface of the liver, somewhat resembling the condition of the lung in acute bronchiectasis. Numerous biliary abscesses may be scattered throughout the liver, both on the surface and in the substance of the organ, and adjacent abscesses may run together and form a confluent or areolar abscess which shows septa of fibrous tissue. On the other hand, there may be a single localised abscess, or only quite a few small abscesses formed of ampulla-like dilatations of the ends of the ducts. The pus is often bile-stained, and may contain soft, calculous matter. The small abscess may leak into the peritoneum and set up general peritonitis or a local peritoneal abscess. In the substance of the liver abscesses may form outside the ducts, possibly in the lymphatics, and suppuration may extend into the branches of the portal vein, setting up pylephlebitis. When this occurs, there is diffuse suppuration of the portal spaces in the liver.

The suppurative process may extend into Wirsung's duct and set up suppurative pancreatitis, and by a further extension of infection to the peritoneum covering the pancreas a local abscess in the lesser sac of the peritoneum—the omental bursa of American writers. Pancreatitis due to gall-stones in the common duct is referred to on page 755. Suppuration may spread from the pancreas into the portal vein and set up pylephlebitis.

The suppurating bile-ducts may leak into the peritoneum and set up either general peritonitis or a local peritoneal abscess. When on the convex surface of the liver, the abscesses may perforate the diaphragm and set up an empyema or bronchobiliary fistula, while abscesses on the under surface may open into the colon or set up a perinephritic abscess (Rogers).

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* Rogers, L.: Brit. Med. Jour., 1903, vol. ii, p. 706.

Microscopically the larger portal spaces are dilated, and relics of their fibrous tissue are visible, but it may be difficult to distinguish the remains of the large bile-ducts from those of the portal veins, since both may be involved in the same suppurative process. The walls of the ducts may be destroyed and replaced by small cells which extend into the surrounding liver substance. There may be comparatively well-formed fibrous tissue from chronic pericholangitis, but the chief feature is diffuse small-cell infiltration. In places the liver cells can barely be recognised, and the condition is that of a commencing abscess.

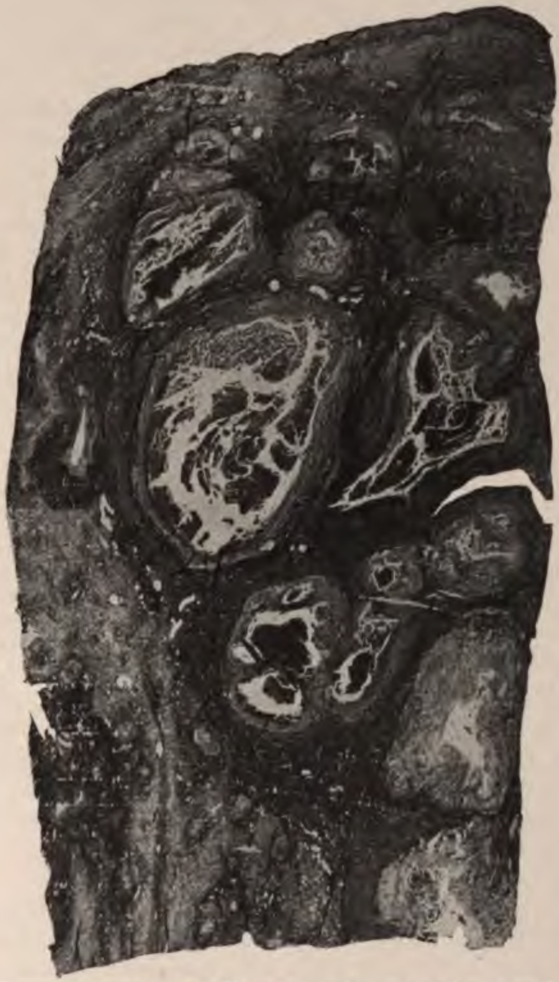

Fig. 83.—Photomicrograph of a Microscopic Section of Liver in Suppurative Cholangitis.

Shows numerous abscess cavities surrounded by condensed fibrous tissue, which appears more darkly stained. It is impossible to make out and distinguish the bile-ducts from the branches of the portal vein, since both are involved. (By Dr. Spitta. Low magnification.)

CLINICAL PICTURE.

The patient is feverish, has rigors, and suffers from loss of appetite, nausea and vomiting, marked prostration, and loss of flesh. The liver, which is found to be much enlarged, smooth, and tender, progressively increases in size as the disease goes on. The spleen is also enlarged. Jaundice is often present, but depends more on the cause of the cholangitis than on the disease itself. Thus jaundice accompanies suppurative cholangitis due to gall-stones, worms in the ducts, rupture of hydatid cysts into the ducts, and is often present when the suppurative process is associated with new-growth involving the ducts. But when there is no independent local condition sufficient to produce jaundice, suppurative cholangitis may run its course without jaundice.* This is difficult to explain at first sight, since in catarrhal cholangitis jaundice is such a prominent feature. It seems reasonable to believe that the absence of jaundice may depend on the hepatic lymphatics, which should carry the bile into the general circulation, being impermeable from inflammatory changes.

In the following case there was only very slight jaundice:

A man aged twenty-nine years was admitted under my colleague, Dr. Penrose, to St. George's Hospital in May, 1897, in an extremely grave condition, with a large tender liver, an anæmic, sallow complexion, slight ascites, and a history that two weeks ago he had had fever and jaundice. Two and a half years ago he had had appendicitis. The temperature was subnormal. At a consultation various opinions were expressed, such as pylephlebitis secondary to appendicitis, suppurative cholangitis associated with calculi, abscess, and rapid new-growth of the liver. The following day an exploratory operation was performed, and a nodule, which might have been either new-growth or early inflammatory change, was cut into. Microscopic examination showed altered liver cells. The patient died two days later. At the autopsy the liver weighed 7 pounds and showed suppurating areas around the bile-ducts in the liver; the larger extra-hepatic bile-ducts contained mucus. There were no calculi in the gall-bladder. The portal vein was normal. The spleen was large and soft, weighing 17 ounces. The appendix was quite normal.

Pain may be due to peritonitis on the surface of the liver set up by suppuration in the ducts under the capsule, and is worse on respiration and on movement. Colicky pain may be set up by factors underlying the acute infection, such as gall-stones, the rupture of hydatids into the ducts, or worms in the ducts. Pseudo-gall-stone colic may also occur when malignant disease involves and obstructs the ducts. In some instances pain is entirely absent.

Septic absorption which gives rise to the severe constitutional symptoms may lead to diarrhœa. From local or general peritonitis secondary to leakage of abscesses on the surface of the liver abdominal distension may come on before death.

Complications.—In addition to local or general peritonitis from leakage or rupture of the suppurating areas, general hæmic infection may occur. Pus and micro-organisms may pass into the hepatic veins and so reach the lungs and give rise to pyæmic abscesses, pleurisy, and empyema. Infective endocarditis may be induced in the same way, and when the infective agents have got into the general circulation, the joints, meninges, etc., may be affected.

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* *Vide* Gilbert and Lereboullet: Bull. et Mem. Soc. Méd. d. Hôp. Paris, 1900. [Les angiocholitis Anicteriques], 3d series, xvii, 477.

Duration.—Suppurative cholangitis may supervene in chronic catarrhal cholangitis, so that the duration is difficult to fix with accuracy. In most cases where the disease comes on acutely it lasts about three weeks. In exceptional instances where the suppurating ducts have discharged into the colon, bronchus, etc., the course of the disease is much prolonged. Thus Rogers * describes cases which lasted eighteen and six months respectively. The importance of drainage in the duration of the disease is shown by the prolonged course of bronchobiliary fistulæ which in the majority of cases are due to suppurative cholangitis.

DIAGNOSIS.

Fever with signs of grave constitutional disturbance in a patient whose liver progressively increases in size and who has had symptoms in the past pointing to gall-stones are the features of importance. Jaundice is not essential, but its presence is in favour of suppurative cholangitis as against suppurative pylephlebitis and tropical abscess.

The **differential diagnosis** must be made from chronic catarrhal cholangitis, from the two other forms of intra-hepatic suppuration,—pylephlebitis and tropical abscess,—from some cases of new-growth associated with fever, and possibly from cases of acute cirrhosis with jaundice.

In chronic catarrhal cholangitis there are periodic attacks of fever, pain, and intensification of jaundice, while in the intervals the patient is comparatively well. In suppurative cholangitis the fever is continuous and there are no intervals of relief: jaundice is less marked, while the patient's general condition is much graver.

Pylephlebitis is accompanied by the same general symptoms and hepatic enlargement as suppurative cholangitis. Jaundice is more frequent, appears earlier, and is more marked in cholangitis, while splenic enlargement is more often prominent in suppurative pylephlebitis. It must be remembered that these two conditions may be combined. In tropical abscess there is often a history of dysentery and there may be fluctuation or local bulging with œdema of the chest-wall. In cases where the abscess is deeply situated the diagnosis is difficult. The history of past dysentery or gall-stones is in favour of single abscess or cholangitis respectively; jaundice, if present, makes cholangitis more probable. But in case of doubt, the rarity of suppurative cholangitis and the relative frequency of abscess must have their due weight. Very rapid new-growth in the liver accompanied by fever and jaundice may very closely resemble suppurative cholangitis; in fact in some cases of new-growth involving the ducts suppurative inflammation of the ducts occurs. In the absence of any definite evidence of new-growth, such as a palpable tumor, the diagnosis may be possible only when the liver is freely exposed. In cases of acute cirrhosis with fever, jaundice, and enlargement and tenderness of the liver the resemblance to suppurative cholangitis is very considerable. In cirrhosis of this type there are usually a marked alcoholic history, splenic enlargement, and hæmatemesis, while the constitutional symptoms are less severe than in suppurative cholangitis.

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* Rogers, L.: Brit. Med. Jour., 1903, vol. ii, p. 706.

PROGNOSIS.

The prognosis depends on the course of the disease; if it remains limited to the large ducts or is operated on early before it has spread to the liver or pancreas, recovery may occur; probably some cases of empyema of the gall-bladder began as suppurative cholangitis, the original lesion having passed away. If it invades the liver and sets up multiple abscesses and diffuse suppuration of the portal spaces, a fatal termination is inevitable; but there may be only a single local area of suppuration in the liver and the outlook is then much better. In addition to its course and complications, much depends on early operation and free drainage. When a bronchobiliary fistula or a communication between the biliary abscess and other hollow viscera, such as the colon or pelvis of the kidney, forms, the free drainage greatly prolongs life and a cure may even result. These cases of fistulæ in fact differ so much from the rapid course of suppurative cholangitis that they are usually considered as a separate condition.

TREATMENT.

The proper treatment is surgical, and consists in obtaining free drainage for the pus; this may be done by opening the dilated ducts, by cholecystotomy, or by opening biliary abscesses on the surface of the liver.

Medical treatment is only palliative, but it may be combined with surgical treatment and then be of distinct use. Salicylate of soda should be given, inasmuch as it is a cholagogue, and by increasing the flow of bile tends to wash out the bile-ducts.

CHRONIC CATARRHAL CHOLANGITIS.

Chronic infective or catarrhal cholangitis may be divided into two forms: (i) That associated with and largely due to cholelithiasis, and (ii) that due to other causes.

The form of chronic cholangitis associated with the presence of a gall-stone in the common bile-duct is so intimately related to cholelithiasis that it is described in connexion with that disease. (*Vide* Intermittent Hepatic Fever, p. 750.) Non-calculous chronic catarrhal cholangitis will be described under two headings: (A) Chronic catarrhal cholangitis of the large, extra-hepatic bile-ducts, and (B) chronic catarrhal cholangitis of the intra-hepatic bile-ducts (angiocholitis).

(A) CHRONIC CATARRHAL CHOLANGITIS OF THE EXTRA-HEPATIC DUCTS DUE TO CAUSES OTHER THAN GALL-STONES.

It may depend on chronic gastro-duodenal catarrh, such as is seen in drunkards. It may occur in the course of malignant disease of the liver or of the bile-ducts, and in the latter condition is more likely to supervene when the growth is at the biliary papilla. Suppuration in the liver or hydatid cysts rupturing into the bile-ducts may set up cholangitis which may be catarrhal at first, but is more likely to become suppurative. Infectious diseases, such as typhoid, influenza, pneumonia, etc., may play some part in the production of chronic catarrh of the bile-ducts. Typhoid fever and influenza may set up an acute cholangitis, and probably this may leave behind it a chronic catarrh. How often they may set up a slight degree of chronic catarrh without any previous acute inflammation it is difficult to say. In these cases the cholangitis is ascending and due to the spread of inflammation or microbic infection from the duodenum. There are some cases of prolonged catarrhal jaundice * which, after hanging fire for weeks and months with intermissions and exacerbations, eventually clear up completely. It seems probable that in these cases there may be an underlying chronic inflammation of the common duct.

Clinical Aspect.—When supervening on acute catarrh the jaundice remains and may arouse the suspicion of malignant disease or of an impacted calculus in the common duct. The chronic jaundice leads to some wasting from malnutrition. It varies in intensity from time to time, becoming more marked after attacks of fever and pain. The general features are those of chronic relapsing jaundice, and are in miniature the same as those of intermittent hepatic fever (*vide* p. 752), to which the reader should refer.

The inflammation may spread upwards to the liver, and in very rare instances be followed by acute yellow atrophy, while from increased virulence of the microbic infection suppurative cholangitis may develop.

The **diagnosis** of chronic catarrhal inflammation of the larger bile-ducts from hypertrophic biliary cirrhosis with chronic jaundice must be made on the absence of the marked hepatic and splenic enlargement.

From a gall-stone in the common duct with chronic infective cholangitis the diagnosis is very difficult, inasmuch as the two conditions are much the same, with the exception of the presence of a gall-stone. In cholelithiasis with infective cholangitis there tends to be more pain, and the attacks of intermittent hepatic fever to be better marked, but not uncommonly there is no history of cholelithiasis, and a differential diagnosis between these two closely allied conditions may not be justified. It is so much commoner to find a gall-stone in the lower end of the common duct in chronic catarrhal or infective cholangitis that this condition should be diagnosed in any doubtful case.

Treatment.—The diet should be simple, and milk should form a large amount of the food. Irritating articles of diet and alcohol must be forbidden. Calomel and saline purges should be given to prevent constipation and minimise gastro-intestinal catarrh; for the latter purpose alone calomel should be given in very minute doses ($\frac{1}{40}$ to $\frac{1}{20}$ gr.) three or four times daily, while salicylates and plenty of water should be taken so as to flush out the bile-ducts. Benefit will result from a visit to a spa, such as Harrogate, Llandrindod, Leamington, Bath, Vichy, Neuenahr, Homburg, Carlsbad, etc.

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* *Vide* Dieulafoy: Sem. Méd., 1888, p. 270.

In prolonged cases in which no benefit follows medical and spa treatment, the question of operating with a view to draining the ducts should be considered. This course is also indicated by the difficulty of eliminating the presence of a calculus in the common duct.

Lejars [*] and Quénu [†] report cases of persistent chronic cholangitis, which were not associated with cholelithiasis, as cured by operation.

It is possible that some of the cases regarded as hypertrophic biliary cirrhosis in which cholecystostomy and drainage have been followed by a cure may have been cases of chronic infective cholangitis.

Guillot [‡] gives a list of 13 cases of chronic hypertrophic biliary cirrhosis or closely allied conditions in which cholecystostomy and drainage were performed, mainly by Delagenière. Recovery followed in 10.

(B) CHRONIC CATARRHAL CHOLANGITIS OF THE SMALL INTRA-HEPATIC BILE-DUCTS.

Our knowledge of chronic cholangitis of the intra-hepatic bile-ducts (or angiocholitis) is very deficient and is largely theoretical. It may be assumed that poisons conveyed to the liver, either by the portal vein in cases of intestinal autointoxication or by the hepatic artery in general hæmic infections and intoxications, may give rise to catarrh of the intra-hepatic ducts; and that this condition complicates other diseases of the liver, such as portal cirrhosis, chronic venous engorgement, hepatitis, and malignant disease. This condition occurs in hypertrophic biliary cirrhosis with chronic jaundice, but all cases of chronic catarrh of the intra-hepatic ducts do not conform to the type of Hanot's disease, though the conditions are allied and require the same general treatment. The small ducts show proliferation of the lining epithelium, which may block up the lumen; there may be some dilatation of the small bile-ducts, and there is pericholangitic fibrosis.

The following conditions were thought to be due to chronic angiocholitis, but at present their pathological nature requires confirmation.

Klippel and Vigouroux [§] describe a case of chronic angiocholitis with hepatic insufficiency, diarrhœa, no jaundice or enlargement of the spleen, in which signs of acromegaly developed. The authors suggest that this was due to hepatic insufficiency in the same way that clubbed (hippocratic) fingers develop in hypertrophic biliary cirrhosis. The liver showed angiocholitis and fibrosis of the portal spaces.

Lereboullet [‖] has described a somewhat similar condition under the name meta-icteric splenomegaly. Jaundice due to angiocholitis occurs first, and subsequently, as it recedes, the spleen becomes enlarged. The enlargement of the spleen is supposed to be due to passive venous engorgement produced by pressure on the branches of the portal vein by sclerosing angiocholitis.

Under the title simple family cholæmia or acholuric jaundice Gilbert and Lereboullet [**] describe a common condition often affecting several members of a family, especially Jews and eastern races, in which jaundice is slight and bile-pigment is present in the blood serum, but not in the urine (acholuria). It is thought to be due to an attenuated chronic biliary infection (*vide* p. 39).

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[*] Lejars: Medical Week, 1897, p. 139. [†] Quénu: Medical Week, 1897, p. 163.

[‡] Guillot: Gaz. hebdom. de Méd. et de Chirurg., Jan. 16, 1902, p. 49.

[§] Klippel and Vigouroux: La presse Médicale, March 21, 1903.

[‖] Lereboullet: Sem. Méd., 1903, p. 180.

[**] Gilbert et Lereboullet: Bull. et Mem. de la Soc. des Hôp., May 30, 1901. Gaz. hebdom. de Méd. et de Chirurg., Sept. 21, p. 809.

The clinical manifestations ascribed to this diathesis are numerous, and include slow pulse, melancholia, and dyspepsia, pigmentation of the skin, a tendency to xanthelasma, pruritus, hæmorrhages, albuminuria, and other manifestations, such as arthritis. In fact, in its catholicity the condition recalls Murchison's conception of lithæmia.

Cases thought to be due to chronic catarrhal inflammation of the small intra-hepatic ducts should be treated with plenty of water and occasional courses of salicylate of soda, so as to wash out the ducts and remove catarrh. Minute doses of calomel ($\frac{1}{40}$ gr.) may be given twice or three times a day to minimise intestinal fermentation, and the bowels should be kept freely open and the diet should be simple and nourishing. Alcohol should be forbidden. Spa treatment on the same lines as in chronic catarrhal cholangitis of the larger ducts may be adopted. The cases of simple family cholæmia described by Gilbert and Lereboullet probably require little more than dietetic treatment and the general directions necessary to prevent constipation and dyspepsia.

PERICHOLANGITIS.

Pericholangitis may be divided into: (*a*) Extra-hepatic, affecting the larger bile-ducts; and (*b*) intra-hepatic. Extra-hepatic pericholangitis may accompany changes in the larger ducts, but is entirely subordinate to that condition.

INTRA-HEPATIC PERICHOLANGITIS.

This is chiefly of pathological interest, since it either occurs as part of other morbid lesions or has no definite clinical associations. It is met with under different conditions and may be acute, as in suppurative cholangitis, of which it forms part, or may be chronic.

Acute pericholangitis cannot be recognised apart from acute inflammation in the portal spaces, such as suppurative cholangitis or pylephlebitis, to which it is, as far as is known, practically always secondary. It is, however, quite conceivable that an acute inflammation of the lymphatic vessels around the bile-ducts might occur independently of cholangitis. It might be set up by an abscess in the liver. But there is no certain knowledge on this point.

Chronic Pericholangitis.—This occurs in several conditions described elsewhere; thus pericholangitis forms part of hypertrophic biliary cirrhosis, there being fibrosis around the smaller bile-ducts from extension of inflammation from their interior. In gall-stone obstruction with infection of the ducts there is a varying amount of fibrosis surrounding the ducts.

In a case of enormous dilatation of the intra-hepatic bile-ducts in which the liver was like a hydronephrotic kidney, there was very marked chronic pericholangitis. (Raynaud and Sabourin.*)

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* Raynaud and Sabourin: Archiv. de Physiol. norm. et path., 1878, p. 37.

In the condition described as tuberculous cavities in the liver the tuberculous processes begin in the loose tissue surrounding the bile-ducts —tuberculous pericholangitis.

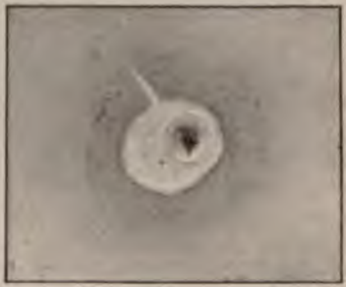

FIG. 84.—Drawing of Naked-eye Appearance of a Section of Liver with Chronic Pericholangitis with Secondary Pylephlebitis.

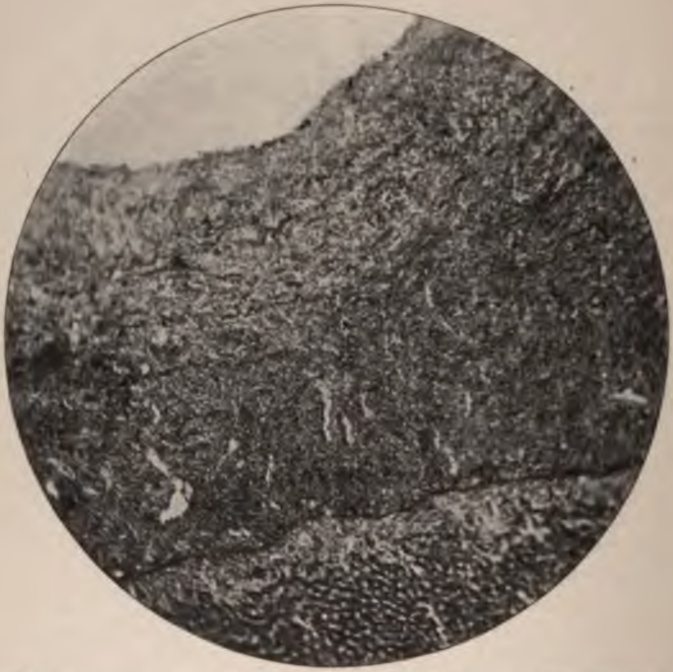

FIG. 85.—Photomicrograph of the White-looking Material Cccupying a Portal Space.

It is composed of granulation tissue. The central space represents the remains of the portal vein, which in this instance was destroyed by secondary suppurative pylephlebitis.

In very rare instances pericholangitis, which is not an entirely subsidiary part of cholangitis, is seen. To the naked eye the portal spaces are occupied by white material which has a very close resemblance to tubercle. Strangeways Pigg and I * described a case, and Morley Fletcher † has since given an account of another. In the first it appeared probable that catarrhal cholangitis had set up chronic pericholangitis, while Fletcher took the view that the pericholangitis was primary. In our case there was secondary suppurative pylephlebitis, while in Fletcher's the portal vein was healthy. It appears probable that the inflammation involves the portal lymphatics; in our case the glands in the portal fissure were much enlarged, and to the naked eye there was some resemblance to lymphadenoma.

The white-looking material in the portal spaces is composed of granulation tissue in various stages of development, and in these two cases were certainly not tuberculous. It contained numbers of bile-ducts, many of which were proliferating and dilated.

Clinically, these cases showed no characteristic features. In Morley Fletcher's case there was bronchiolectasis, and in our case the patient had advanced renal disease and several attacks of hæmorrhage from the bowels.

In neither of these cases was there jaundice; this can to some extent be explained by supposing that blocking of the lymphatics prevented the absorption of bile by the lymph-channels.

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* Rolleston and Strangeways Pigg: Journ. Path. and Bacteriol., vol. v, p. 221, 1898.

† Morley Fletcher: Trans. Path. Soc., vol. lii, p. 193.

PARASITIC AFFECTIONS OF THE BILE-DUCTS.

ASCARIS LUMBRICOIDES.

A round worm in the duodenum may work its way into the biliary papilla and common bile-duct and give rise to biliary obstruction and infection of the ducts. Cases have been described in which jaundice has disappeared after the passage of a bile-stained round worm; and it has been reasonably assumed that in some instances the head of the worm has temporarily blocked the lower end of the bile-duct.

Mertens * collected 48 cases of round worms in the bile-ducts, and more recently Sick † has brought together 64 cases. From the frequency of ascarides in the young it is natural that some of the cases of bile-duct infection are in children.

The worms dilate the bile-ducts, carry micro-organisms with them, and, by infecting the bile-passages, give rise either to suppurative cholangitis or to single or multiple abscesses in the liver.

Roud ‡ described a case where streptococci and colon bacilli were found in the hepatic abscesses, which also contained air.

In five of Mertens' cases gall-stones were associated with the presence of round worms. Hanot § regards the cholelithiasis as due to the infective agency of the worms. In his own case Mertens believed that the passage of a calculus assisted the entrance of the worm by dilating the passage.

The following case, recorded by Dr. John Davy, ‖ is one of the earliest and illustrates the condition well. A Maltese boy aged two years who died from dysentery was found to have numerous round worms in the stomach, small intestines, colon, and liver. The common and hepatic ducts were distended with worms, and there were several abscesses in the liver, containing worms.

There is an excellent specimen (No. 533) in the Cambridge Pathological Museum showing the common bile-duct distended with Ascaris lumbricoides. The patient was a child. The duct is so tightly distended that jaundice must have been produced, though there is no history of the case.

The **clinical aspects** are those of enlarged liver, jaundice, fever, attacks of biliary colic, and, in a word, are those of infective cholangitis with biliary obstruction. In only 2 of 48 cases collected by Mertens was a diagnosis made during life. The diagnosis depends on finding the worms or their ova in the dejecta; otherwise the cases are likely to be regarded as due to gall-stones.

Treatment.—Santonin should be given if the presence of round worms is suspected. In the presence of signs of infection of the common duct the duct should be cut down upon and drained. In a case diagnosed as a calculus in the common duct recovery followed choledochotomy. (Neugebauer.*)

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* Mertens: Deutsch. med. Wochen., Bd. xxiv, S. 358, 1898.

† Sick: Inaug. Dissert., Tübingen, 1901. Quoted by Neugebauer: Archiv f. klin. Chirurg., Bd. lxx, S. 584, 1903.

‡ Roud: Thèse, Lausanne, 1896.

§ Hanot: Archiv. Général. de Méd., tome clxxvii, p. 74.

‖ Davy, J.: Diseases of the Army, p. 423, 1862.

DISTOMA.

Several species of distomida may be met with in the bile-ducts of the liver in man.

Distomum hepaticum is commonly found in sheep, and gives rise to the disease known as sheep-rot, which has proved disastrous to so many sheep-farms. In very rare instances men have become infected from taking water or vegetables contaminated with the dejecta of sheep suffering from the disease. Infection with Distomum hepaticum may arise in this country, which is not the case with the other varieties of distoma.

As far back as 1857 Budd, who added an appendix to his work on the liver, dealing with distoma and their morbid effects in sheep, quoted three cases of distoma in the biliary tract of man.

Invasion of the ducts by distoma is much commoner in tropical countries, such as China, Japan, and India. *Distomum sinense* is found in India, China, Japan, and Tonkin. In Japan 20 per cent. of the inhabitants in certain low-lying districts are affected. (Baelz.†) *Distomum lanceolatum* and *Distomum conjunctivum* have been met with in the bile-ducts of human beings, but are of no real pathological importance.

Morbid Anatomy.—The distoma cling by their suckers to the mucous membrane of the bile-ducts, which become dilated and inflamed and contain mucus and the ova of the worms. Cystic dilatations varying from the size of hazel-nut to a walnut may form in the course of the ducts. Fibrosis from pericholangitis spreads out from the portal spaces and the liver cells may be compressed. Suppuration may occur in the dilated bile-ducts. The liver is enlarged. Scheube ‡ suggests that the form of biliary cirrhosis so common in native Indian children around Calcutta is due to distoma, but does not give any proof in support of this view.

Clinical Aspect.—Though sometimes the worms remain latent, some of the following symptoms and signs may be expected: Hepatic pain and enlargement of the liver, jaundice, gastro-intestinal disturbance, vomiting, diarrhœa, or constipation, fever, enlargement of the spleen, ascites, œdema of feet, and anæmia. The cases may terminate as suppurative cholangitis or abscess in the liver, and the prognosis is, therefore, bad. The diagnosis depends on the detection of the ova in the stools. The treatment consists in giving vermicides, such as Filix-mas and purgatives. When there are signs of suppurative cholangitis, the common bile-duct should be opened.

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* Neugebauer: Archiv f. klin. Chirurg., Bd. lxx, S. 584, 1903.

† Berlin. klin. Wochen., 1883, S. 234.

‡ Scheube: Diseases of Warm Climates, p. 364. English translation, 1903.

PSOROSPERMOSIS.

The invasion of the bile-ducts of the rabbit by psorosperms or the Coccidium oviforme is extremely common, and leads to the production of papillomatous growths from the mucosa of the dilated ducts, which are a beautiful demonstration of the irritating effects of a parasite. On section, the liver shows a number of white, caseous areas closely resembling tubercles to the naked eye. These appearances have been often described, and reference may be made for a detailed account of the parasite and its effects to Delépine's[*] paper. Sometimes, as the result of secondary infection, acute inflammation is set up in the ducts and the mucous membrane becomes replaced by granulation tissue—psorospermial cholangitis.

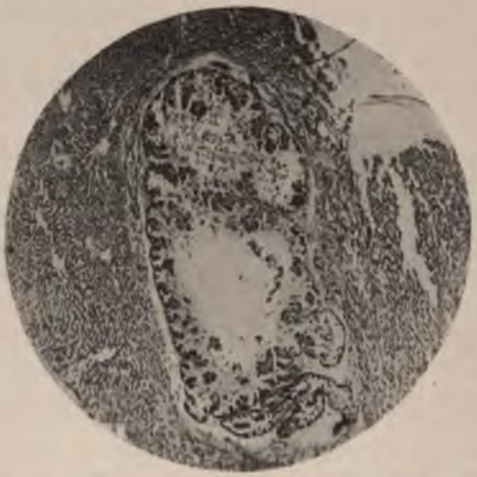

Fig. 86.—Shows Section of Rabbit's Liver Under a Low Power, with Papillomatous Growths in the Dilated Bile-duct due to the Irritation of Psorosperms. (Photomicrograph by S. G. Penny, Esq.)

Psorospermial invasion of the human liver is very rare, but it has been more often described in the liver than in any other internal organ of the human body. McFarlane[†] collected 20 cases of human psorospermosis, and, omitting supposed psorospermial affections of the skin, such as Darier's disease, found that the liver was affected 11 times, the intestines 5 times, the kidneys twice, and the pleura and spleen once each.

A case of calcification of a psorospermial tumor removed during life from a patient who was thought to have a calcified gall-bladder is put on record by Carrel.[‡] In Silcock's[§] case there was considerable enlargement of the liver, which weighed 83 ounces. The spleen and intestines were also affected, and psorosperms were cultivated for two months. Podwyssozki[‖] has reported 4 cases.

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[*] Delépine: Trans. Path. Soc., vol. xli, p. 348.

[†] McFarlane: Journ. of Applied Microscopy (Rochester, U. S. A.), 1898, vol. i, p. 41.

[‡] Carrel: Lyon Médical, tome xciii, p. 89, 1900.

[§] Silcock: Trans. Path. Soc., vol. xli, p. 320.

[‖] Podwyssozki: Centralbl. f. Bakt. u. Parasit., 1889, Bd. vi, S. 41.

It is, however, not unlikely that some cases have been overlooked and the lesions regarded as caseous tubercle, and that a microscopic examination, if undertaken, would have revealed the presence of psorosperms. The coccidia are taken in food, multiply in the stomach, and invade the common bile-duct.

Clinical Aspect.—In the human subject the symptoms are obscure. In some cases there have been fever, enlargement and tenderness of the liver without jaundice, and prostration. In rabbits increase in the number of eosinophile leucocytes has been observed (Federici *), but I am not aware that this has been observed in man.

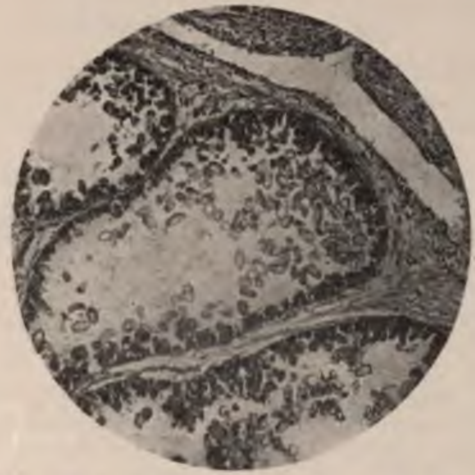

FIG. 87.—THE SAME SECTION UNDER A HIGH POWER, SHOWING THE COCCIDIA LOOSE BY THE DILATED BILE-DUCT. (Photographed by S. G. Penny, Esq.)

PENTASTOMA CONSTRICTUM.

This parasite gains entrance to the alimentary canal, and, reaching the liver, gives rise to cysts, especially in the neighbourhood of the falciform ligament, which are thought to be dilated bile-ducts. The cysts contain clear fluid and a single coiled-up parasite, which may be alive at the time the liver is examined after death. The walls of the cyst are composed of firm fibrous tissue and have a great tendency to undergo calcification. The peritoneum in the neighbourhood of the cysts may show considerable inflammation, and infection of the lungs may occur. It is remarkable that though the parasite gives rise to inflammation of the peritoneum and lungs, it does not appear to irritate the intestines and liver.

Cysts containing the parasite have been observed in the liver by

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* Federici: Rivista crit. di Clin. Med., Aug. 23, 1902.

Pruner,[*] Aitken,[†] Girard,[‡] Chalmers.[§] It is said to occur only in negroes, but this is not correct, as there is a specimen of a liver showing five cysts containing the parasite, in the museum at Netley (No. 1244), taken from an English soldier who died of spinal caries. Similar cysts containing the Pentastoma denticulatum have occasionally been met with in patients dying from other causes.

PARAMŒCIUM COLI.

Synonym: Balantidium coli.

This parasite is very common in the colon of the pig, and has been found in the intestines of man in association with diarrhœa. In the following unique case the parasite was found in the liver of man:

In a man aged fifty-nine years who died with carcinoma of the pylorus Russell and Buzzard[‖] found a dozen cysts the size of peas and containing living paramœcia in the liver. The cysts, which had firm fibrous walls, were probably derived from the bile-ducts and due to the irritation set up by paramœcia which had travelled up the bile-ducts from the duodenum. The cysts did not show any papillary growths resembling those in psorospermosis of the liver. Inasmuch as the patient died from gastric carcinoma, it is not improbable that an absence of HCl in the gastric juice allowed these organisms to develop in the stomach. No proof of this, however, is forthcoming, as the vomit was not examined.

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[*] Pruner: Krankheiten des Orient, 1847, S. 245.
[†] Aitken: Science and Practice of Medicine, vol. i, p. 650, 1868.
[‡] Girard: Compt. rend. Soc. biolog. Paris, 1896, tome x, p. 469.
[§] Chalmers: Lancet, 1899, vol. i, pp. 1715, 1729.
[‖] Trans. Path. Soc., London, vol. l, p. 149.

INNOCENT TUMORS OF THE BILE-DUCTS.

Innocent tumors of the bile-ducts are both rare and of little importance. It is noteworthy that while innocent growths are almost equally rare in the bile-ducts and in the gall-bladder, primary malignant disease is much commoner in the gall-bladder.

PAPILLOMA.

Very few examples of papillomata of the larger extra-hepatic bile-ducts are on record, but it is probable that the condition is not quite so exceptional as the number of instances put on record would lead one to believe. Some of the cases described as malignant, but not examined microscopically, may have been innocent.

Chappet * speaks of a case as carcinoma, but goes on to say that the growth was developed at the expense of the mucosa, which was not ulcerated, and that the other coats of the duct were little or not at all affected, so that it may have been an innocent papilloma.

As the résult of extensive mucoid change taking place in papillomata of the bile-ducts a condition might be produced such as that described by Wilks and Moxon † in a child aged four years whose common bile-duct, dilated to the size of its head, contained pendulous myxomatous growths with muscular fibres in them. The small fatty growths described by Wardell ‡ as obstructing the cystic and common bile-ducts might also be regarded as originally papillomata of the bile-ducts, which subsequently underwent myxomatous degeneration and then, from bile-staining, took on a yellowish tinge, suggesting fat; for no microscopic examination appears to have been made. Devic and Gallavardin § quote similar cases of lipomata arising from the mucosa of the bile-ducts recorded by Ehrmann and by Dickmann. Submucous lipomata occasionally arise in the intestines, so it is quite possible that the same growth might be found in the bile-ducts.

A papillomatous growth from the inside of the common bile-duct, analogous to a duct papilloma in the breast or to a polypus of the intestine, was removed by Sir W. Bennett from a patient at St. George's Hospital. It was close to a gall-stone that had been impacted for two months. ‖ It was a branching papilloma, composed of a basis of fibrous tissue covered over by columnar epithelium. In places the connective tissue had undergone mucoid degeneration. The after-history of the patient, however, rather suggested that she had malignant disease. (*Vide* p. 684.)

The papillomatous growths in rabbits' intra-hepatic bile-ducts, due to the irritation of psorosperms, are extremely common and well known, but a similar lesion in man is a pathological curiosity. A case of cystic tumors of the bile-ducts in man due to the irritation of these coccidia has been recorded by Podwyssozki.*

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* Chappet: Lyon Médical, t. lxxvi, p. 146.

† Wilks and Moxon: Pathology, p. 485, 3d ed., 1889.

‡ Wardell: Lancet, 1869, vol. ii, p. 407.

§ Devic and Gallavardin: Rev. de Méd., July, 1901, p. 570.

‖ Rolleston: Trans. Path. Soc., vol. xlv, p. 83, and Medical Chronicle, Jan., 1896.

Papillomatous growths of the intra-hepatic ducts are the same as adenomata, under which name they are sometimes described. They may be multiple and give rise to no symptoms. On the other hand, there may be a single tumor, and in either case they may become cystic. (*Vide* Adenoma of Bile-ducts.)

Simple papillomata are occasionally seen around the biliary papilla in the duodenum, but are growths of the intestinal surface of the papilla and not of the bile-duct. Papillomata may, however, arise in the cavity of the diverticulum of Vater. Macphedran † has described a case which, like most of the cases of papillomatous growths around the duodenal orifice of the biliary papilla, gave rise to suppurative cholangitis.

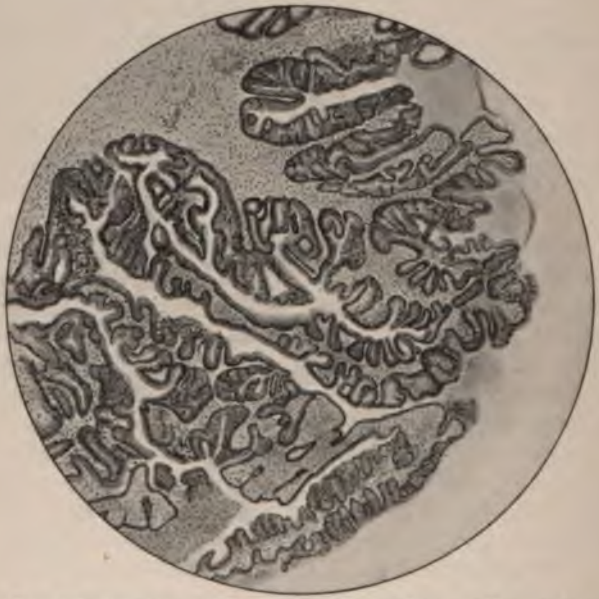

FIG. 88.—DRAWING OF PAPILLOMA OF THE COMMON BILE-DUCT.
There is some adherent mucus on the surface of the growth. There is myxomatous degeneration of the fibrous core of the papilloma. (From the case referred to in the text, p. 681.) × 40.

Hydatid Cysts.—Devic and Gallavardin ‡ quote three cases where hydatid cysts arose in the walls of the bile-ducts, recorded by Cadet de Gassicourt, Ignatieff, Macready.

A *fibroma* the size of a bean obstructing the lumen of the bile-duct has been described,§ but the condition is practically unique, and it is possible that it was carcinomatous.

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* Podwyssozki: Centralbl. f. Bakt. u. Parasit., 1889, Bd. vi, S. 41.

† Macphedran, A.: Sajous' Annual, 1899, vol. iv, p. 422.

‡ Devic et Gallavardin: Rev. de Méd., July, 1901, p. 571.

§ Albers, quoted in von Ziemssen's Cyclopædia of Practical Medicine, vol. ix, p. 569, 1880.

MALIGNANT DISEASE OF THE LARGER (EXTRA-HEPATIC) BILE-DUCTS.

Under this heading primary malignant disease of the extra-hepatic bile-ducts will be dealt with. When carcinoma arises, as it probably does in an appreciable number of instances, in the small intra-hepatic bile-ducts, the condition is, for all practical purposes, primary carcinoma of the liver. Secondary growths very rarely occur in the bile-ducts, though in multiple malignant growths of the peritoneum the bile-ducts may be invaded from without. Extension of growth to the bile-ducts from the hilum of the liver, from carcinomatous glands in the neighbourhood, from the lesser omentum, or from the pancreas are referred to elsewhere. Primary carcinoma of the ampulla or diverticulum of Vater, into which the common bile-duct and Wirsung's duct of the pancreas open, is very much the same as primary carcinoma of the lower end of the common bile-duct, but a separate description of this condition is given on page 697.

Incidence.—Malignant disease of the large or extra-hepatic bile-ducts is probably not so rare as has been thought, or as might be gathered from the cases put on record in the past. It is noticeable that within the last fifteen years the number of cases described has increased four-fold.

In 1889 Musser * collected 18 cases; in 1897 P. Claisse † tabulated 50; in 1901 Devic and Gallavardin,‡ after excluding doubtful cases, analysed 55 examples, and I have notes of 80, about which there seems no doubt.

The disease is doubtless commoner than is thought, since it may be overlooked or more probably described as something else. Thus some of the cases recorded as malignant disease of the lesser omentum probably originated in the bile-ducts. Carcinoma of the pylorus may, of course, spread up into the gastro-hepatic omentum, but if there is no primary source such as this for carcinoma of the lesser omentum, the common bile-duct should be suspected and carefully examined.

Again, in some of the cases described as primary malignant disease starting in the portal fissure and involving the bile-ducts the growth may well have started in their walls.

In other instances a slow-growing fibrous carcinoma of the bile-ducts has probably been described as a simple cicatricial stricture. In fact, to the naked eye there may be so close a resemblance that a microscopic examination is necessary to settle the question.

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* Musser, J. H.: Boston Med. and Surg. Journ., vol. cxxi, p. 581.
† Claisse, P.: Gaz. des Hôp., 1897, p. 1279.
‡ Devic and Gallavardin: Rev. de Méd., 1901, p. 557.

ETIOLOGY.

Zenker* believes that in the case of the gall-bladder a papilloma or an adenoma first develops and subsequently becomes transformed into an adenocarcinoma. I have seen one case which suggests that the same sequence might occur in the bile-duct.

A papilloma was removed during a choledochotomy from the bile-duct of a woman, the growth being in immediate contact with a gall-stone which had been impacted for about two months. Some months later the patient returned with signs compatible with the view that the growth had recurred in the region of the operation wound, but did not remain under observation. I showed the specimen to the Pathological Society † as an example of a papilloma due to irritation of a gall-stone; later on, after the patient's return, the question arose whether, supposing the recurrence to be carcinomatous, the growth had been malignant from the first, or whether the growth had subsequently invaded the duct-walls after the manner of a duct carcinoma in the breast. At the time of the operation there was no sign of any infiltration of the bile-duct, so that if the recurrent growth was carcinomatous, it would appear that a transformation from a simple to a malignant adenoma had taken place.

It is quite conceivable that carcinoma may supervene on an ulcer of the bile-duct, just as it does on an old gastric ulcer.

In a woman aged fifty-seven there was marked stenosis of the lower end of the bile-duct, thought to be due to cicatrisation of an ulcer set up by a gall-stone. Microscopically there was some carcinomatous invasion of the wall. (Krokiewicz.‡) On the other hand, there is no proof that it was not a carcinoma from the first which had subsequently ulcerated.

Relation to Gall-stones.—In carcinoma of the gall-bladder there is a very close association between the presence of gall-stones and carcinoma of the organ. The percentage of gall-stones in cases of carcinoma of the gall-bladder has been put as high as 95 per cent. (Siegert §.) In primary carcinoma of the bile-ducts there is a marked contrast, gall-stones being much less frequently met with.

Thus in 40 cases collected by Devic and Gallavardin ‖ gall-stones were present in only nine instances—six times in the gall-bladder and on three occasions in the bile-ducts; in one case only was the growth found to surround a calculus. In 62 of my cases in which a definite statement as to the presence or absence of gall-stones was made they were present in 23 and absent in 39. It is probable that in a high proportion of the cases where no statement was made gall-stones were absent.

The fact that gall-stones are not so commonly met with in bile-duct carcinoma strongly supports the conclusion, formed on experimental grounds (Mignot **), that calculi are not formed simply as a result of stagnation of bile due to obstruction set up by the growth. Stagnation is much more marked in bile-duct carcinoma than in similar disease of the gall-bladder, and calculi are less common.

Sex.—In 75 cases, in which the sex is recorded, 44 males and 31 females were affected. This contrasts with carcinoma of the gall-bladder, in which females are attacked four times more frequently than males.

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* Zenker: Deutsch. Archiv f. klin. Med., Bd. xliv, S. 159.

† Trans. Path. Soc., vol. xlv, p. 83.

‡ Krokiewicz: Wien. klin. Wochen., March 21, 1898, S. 320.

§ Siegert: Virchow's Archiv, Bd. cxxxiii, S. 353.

‖ Devic et Gallavardin: Rev. de Méd., July, 1901, p. 575.

** Mignot: Archiv. général. de Méd., Aug.-Sept., 1898.

Age.—Primary malignant disease of the bile-ducts usually occurs after fifty years of age. This was so in 52 of my 73 cases. In Musser's 18 cases the average age was 56.6 years, and in my 73 cases 55.7 years; in my series the average age was practically the same in the two sexes (55.7 in males, 55.6 in females); the extremes were 81 years in a woman and 29 in a man.

MORBID ANATOMY.

Situation of the Growth.—Carcinoma may arise in any part of the larger bile-ducts, but it is very rarely observed in either of the two hepatic ducts.

In 80 cases the situation of the growth was as follows:

Common bile-duct:	
Lower end	21
Middle part	11
Junction of common bile-duct, cystic, and common hepatic ducts	25
Common hepatic duct	18
Right or left hepatic ducts	3
In cystic duct	1
In cystic duct and in lower end of bile-duct	1

For the group of cases in which the growth is limited to the common hepatic duct or its two branches, the right and left hepatic ducts, P. Claisse * has suggested the term juxtahepatic.

Of this form of primary carcinoma of the ducts Lecène and Pagniez † have been able to collect only 12 examples. Ingebrans,‡ dealing with practically the same cases, tabulated 16. When juxtahepatic carcinoma attacks the lower end of the common hepatic duct, it readily spreads to and occludes the cystic duct and so becomes carcinoma of the junction of the common, cystic, and hepatic ducts. Devic and Gallavardin § adopt a slightly different classification and divide their 54 cases into two groups: (*a*) Those where the growth was in the common duct, or supraduodenal, 22 cases; and (*b*) juxta, or subhepatic, 32 cases; among this latter category are included cases of growth at the junction of the common bile, common hepatic, and cystic ducts, of which they give no less than fifteen.

When the cystic duct alone is affected, the condition is, both anatomically and clinically, much the same as carcinoma of the neck of the gall-bladder, and is, therefore, more conveniently grouped with carcinoma of the gall-bladder. Very few cases of carcinoma limited to the cystic duct have been recorded; this is probably due to the facts that it either begins close to the gall-bladder and so spreads to it, or that it has extended into the junction of the common hepatic and common bile-duct by the time that the anatomical facts can be investigated.

Appearance of the Growth.—The growth is firm and white, and nearly always small—not larger than a cherry.

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* Claisse, P.: Presse Médicale, Nov. 6, 1897.

† Lecène and Pagniez: Archiv. général. de Méd., 1901, t. clxxxvii, p. 176.

‡ Ingebrans: Archiv. général. de Méd., Sept., 1902, t. cxc, p. 268.

§ Devic and Gallavardin: Rev. de Méd., August, 1901, p. 661.

Large growths are most exceptional—I have seen one as big as an orange. In rare instances the growth may form a rather diffuse, infiltrating mass around the structures in the portal fissure, as in a case described by Planteau and Cochez.*

The growth may be villous on its internal surface, but this appearance may be removed by ulceration; in connexion with this villous nature of the tumor it is of interest to refer again to the possibility that it may start as an innocent papilloma of the lining membrane of the duct. Carcinoma infiltrates the walls of the duct and forms a firm annular stricture; this localised form is the one usually met with. Occasionally the growth extends in the walls of the ducts, and then transforms them into thick, rigid tubes. By this process a considerable extent of the common bile-duct or even of the cystic or common hepatic ducts as well may be converted into carcinomatous tubes.

In some instances the growth projects considerably into the lumen, and may thus produce obstruction rather than by an annular stricture.

In one instance two apparently independent growths were found at the same time in the extra-hepatic bile-ducts.

Carcinoma of the common bile-duct produces complete biliary obstruction during life; after death, however, the stricture does not always appear to be absolutely impervious. It is probable that during life added muscular spasm makes the obstruction absolute.

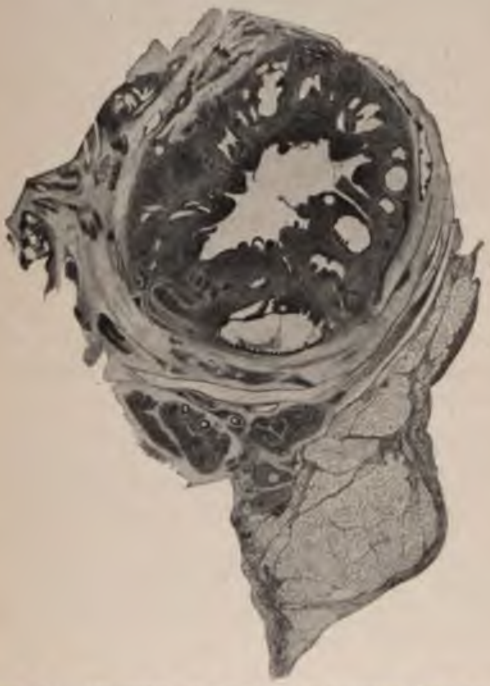

FIG. 89.—DRAWING OF SECTION OF COMMON BILE-DUCT WITH PRIMARY CARCINOMA.

The growth projects into the lumen of the duct and narrows it. The muscular walls of the duct are infiltrated with growth. × 6.

Hæmorrhage occasionally takes place in connexion with the growth. It may be due to cholæmia, to erosion of a blood-vessel, or possibly to acute hæmorrhagic pancreatitis. In the following case, which I examined postmortem, there was a terminal hæmorrhage in the neighbourhood of the pancreas:

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* Planteau and Cochez: Rev. de Méd., Jan., 1903, p. 70.

A man aged forty-one began to suffer from flatulence in 1891 without any colic. In the autumn of 1892 he gradually became thin, weak, and jaundiced. He was admitted to St. George's Hospital under the care of Dr. Whipham on December 17, 1892, deeply jaundiced, with itching of the skin, distaste for fatty food, and general weakness. The liver was enlarged, and the motions devoid of bile. During May, 1893, his legs became œdematous and the loss of strength more apparent. On May 18th he was attacked with abdominal pain, the abdomen became distended and tender; delirium supervened, and hæmorrhages appeared on the legs before death. At the autopsy there was a columnar-celled carcinoma of the lower end of the common bile-duct, which projected down into the duodenum and extended upwards as far as the cystic duct. There were no gall-stones in the gall-bladder. There were secondary nodules of growth under the serous coat of the gall-bladder and in the aortic lymphatic glands, but none elsewhere. The liver was enlarged, and the ducts dilated and full of greenish, watery fluid. The gall-bladder was greatly dilated with greenish fluid, unlike bile. There was a large recent hæmorrhage around the head of the pancreas and the bile-duct, which had dissected its way up between the layers of the mesentery.

Behaviour of the Growth.—The growth is usually small, and does not tend to infiltrate adjacent parts widely. It may grow into the substance of the pancreas, liver, or the portal vein. When the pancreas is invaded, the resemblance to primary malignant disease starting in the head of that gland is very close. Histologically, the primary pancreatic growth is almost always spheroidal, while that in the ducts is columnar-celled carcinoma.

Carcinoma of the duct may directly infiltrate the portal vein and give rise to portal thrombosis. As already mentioned, the growth may project into the lumen of the duct and thus obstruct it. It may extend along the walls of the ducts so as to involve widely the mucous membrane of the biliary tract, or it may spread along the lymphatics in the outer coats of the ducts and thus pass into the liver.

In one case under the care of my colleague, Dr. Penrose, in St. George's Hospital, a growth at the junction of the common bile, cystic, and common hepatic ducts spread up along the side of the hepatic ducts into the liver and produced a second stricture of the left hepatic duct inside the transverse fissure. In Planteau and Cochez's * case, which was of much the same nature, a growth inside the left lobe of the liver was shown to be an expansion of a continuous carcinomatous infiltration spreading along the ducts.

Naked-eye Diagnosis of Primary Carcinoma of the Bile-ducts.—Wherever it starts, the growth may spread along the ducts; thus a considerable extent of the common duct, together with the common hepatic duct and its branches, may be affected at the same time, or the gall-bladder, cystic duct, and the common bile-duct may be infiltrated in continuity. In such cases it is difficult or impossible to determine its starting-point.

Carcinoma of the lower end of the bile-duct may spread to the head of the pancreas, and so present much the same naked-eye appearances as carcinoma of the head of the pancreas involving the common bile-duct. It is probable that some cases described as carcinoma of the head of the pancreas in reality started in the bile-duct. Microscopic examination shows that pancreatic carcinoma is spheroidal-celled, while that of the bile-duct is almost always columnar-celled, and thus provides a criterion for deciding the origin of the growth in any doubtful case.

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* Planteau and Cochez: Rev. de Méd., Jan., 1903, p. 70.

As pointed out above, carcinoma of the bile-ducts at their exit from the liver merges into primary carcinoma of the liver; carcinoma of the cystic duct resembles malignant disease of the gall-bladder; some cases of carcinoma of the common bile-duct have probably been described as cancer of the gastro-hepatic omentum; and carcinoma of the lower end of the bile-duct may closely resemble disease of the head of the pancreas. The disease is probably, therefore, less rare than is usually thought.

On the other hand, it must not be forgotten that malignant disease of the gall-bladder, or more rarely of the pancreas, may spread for a very considerable distance along the course of the bile-ducts.

Thus in a remarkable case of a woman aged fifty-six years under the care of my colleague, Mr. (now Sir) W. H. Bennett, in St. George's Hospital, a spindle-celled sarcoma which began in the gall-bladder spread down along the cystic and common bile-ducts as far as the biliary papilla. In a case of Rose Bradford's * carcinoma extended from the gall-bladder along the cystic duct into the common bile-duct and hepatic duct, the growth terminating abruptly in all directions.

When carcinoma arising in the head of the pancreas involves the common bile-duct and spreads along its walls beyond the confines of the pancreas, it may be difficult or impossible to be certain of the starting-point of the growth until a microscopic examination is made, a spheroidal-celled carcinoma indicating its pancreatic origin. Durante † describes such a case in which the growth appeared to invade the duct from without.

Microscopical Appearances.—Primary malignant disease of the bile-ducts is always a carcinoma, and in the great majority of instances a columnar-celled growth derived from the surface epithelium.

In 38 cases which I have analysed the tumor was a columnar-celled carcinoma in 33; spheroidal-celled in 4; and colloid in one (Leith's ‡). In many cases the description is too vague to base any opinion on, the growth being spoken of as "scirrhus," "encephaloid," or merely as carcinoma.

It is possible that spheroidal-celled carcinoma of the bile-duct may be derived from mucous glands in its wall. Mucoid degeneration of the columnar cells leading to distension of the alveoli is not uncommon.

In a certain number of the cases of columnar-celled carcinoma there is a transition to a spheroidal-celled character; this change is commonly seen in carcinoma of other organs, such as the mamma and gall-bladder, and probably depends on increased rate of growth. It is often described as an atypical carcinoma. In rare cases mucoid or allied degenerative changes in the epithelial cells induce a swollen, flattened appearance, and as a result of the invagination of these cells an appearance closely resembling squamous-celled carcinoma is presented. A similar condition occurs in primary carcinoma of the gall-bladder, where it is discussed. (*Vide* p. 621.)

I am indebted to Dr. W. C. Bosanquet for the section from which the accompanying drawing was made. In some parts of this section alveoli formed by flattened epithelial cells contained cholesterin crystals.

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* Bradford, J. R.: Brit. Med. Journ., 1898, vol. ii, p. 1555.

† Durante: Bull. Soc. Anat. Paris, 1893, p. 342.

‡ Leith: Trans. Med.-Chirurg. Soc., Edinburgh, vol. xv, p. 59.

The supporting stroma of the growth is formed of well-formed fibrous tissue, showing that it is a slow-growing tumor.

Condition of the Bile-ducts.—Below the growth the ducts are of their normal calibre; it is possible that an impacted calculus might be situated below the growth and distend the distal portion of the duct. Above the growth the ducts are dilated, sometimes to such an extreme degree as to allow a finger or a thumb to be introduced. Dilated bile-ducts containing mucus, or in the early stages bile, may project as elevations on the surface of the liver. In rare instances infective cholangitis is present.

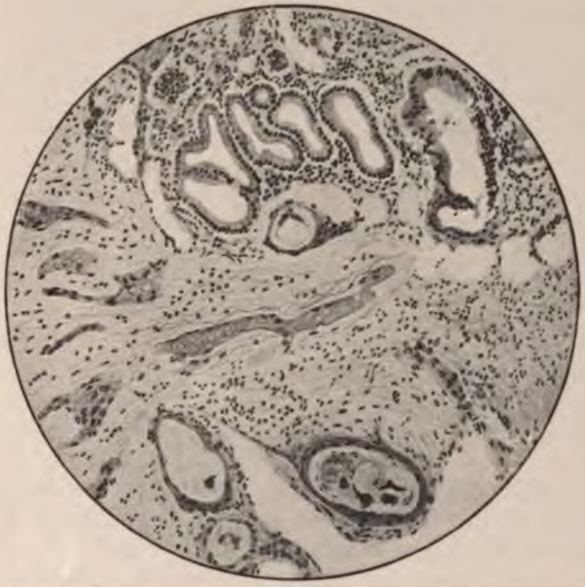

FIG. 90.—MICROSCOPIC DRAWING OF CARCINOMA OF THE COMMON BILE-DUCT.

The growth is columnar-celled in one part, but has the appearance of a squamous-celled growth in others. The latter is an exceptional appearance. (From a specimen lent by Dr. W. C. Bosanquet.)

Condition of the Gall-bladder.—When the growth is in the common bile-duct, the gall-bladder is distended; the only exception to this is, when, from former cholelithiasis, the gall-bladder has been bound down by adhesions and retracted on itself.

In 18 cases where the growth was in the common bile-duct the gall-bladder was distended in 17 (Devic and Gallavardin).

When the growth is in the common hepatic duct, the gall-bladder is nearly always small; in exceptional instances it may be distended with mucus from concomitant obstruction of the cystic duct, or may be occupied by a number of gall-stones. When the growth is situated at the junction of the cystic, common hepatic, and common bile-ducts, the gall-bladder is, as a rule, not enlarged, but from irregularities and variations in the degree of obstruction to the different ducts corresponding differences in the condition of the gall-bladder are met with.

Secondary growths are not very common, probably because the primary growth proves fatal from cholæmia before there is sufficient time for extensive metastases. They are most often found in the liver. In 52 cases the liver was affected in 11. Secondary growths may also arise in the adjacent lymphatic glands and in the peritoneum; in the latter situation they may produce ascites. Secondary growths very seldom occur when the primary growth is in the common hepatic duct or in either of the two hepatic ducts (juxta-hepatic form of carcinoma of the bile-ducts). In 12 cases of juxta-hepatic carcinoma of the bile-ducts analysed by Lecène and Pagniez * there was no instance of a secondary growth.

The liver shows dilatation of the bile-ducts, first with bile, but later with clear mucoid fluid. The organ is atrophied and of a very deep green colour. The liver cells atrophy, and there are areas of icteric necrosis.

According to Fütterer,† this icteric necrosis occurs in the central zone of the lobule, the intermediate and the peripheral zones remaining normal. This is explained on the theory that the distension of the interlobular bile-ducts compresses the interlobular channels and reverses the direction of the flow of bile. The bile then flows into the perivascular lymphatics around the central vein, and sets up necrosis of the neighbouring liver cells.

The liver cells contain bile-pigment, which may be regarded as being in the radicles of the bile capillaries. Around the necrosed areas small-cell infiltration and the formation of so-called new bile-ducts are sometimes seen. The pseudocanalicular formation, which is by no means always present, is an attempt at compensation on the part of liver cells.

In the majority of cases there is no cirrhosis or fibrosis as the result of biliary obstruction. The atrophy of the liver cells allows the existing fibrous tissue to appear more prominent, and has led some writers to believe that biliary obstruction produces hepatic fibrosis. In cases where the ducts have been infected there may be pericholangitic fibrosis. It is conceivable that hepatic cirrhosis may have existed prior to the development of malignant disease of the bile-ducts, or that some fibrosis around the ducts may have been induced by cholangitis due to gall-stones.

Microbic infection of the ducts, which is disposed to by stagnation in the bile channels, may give rise to a pericholangitic cirrhosis, or, if more acute, to suppurative cholangitis, empyema of the gall-bladder, and febrile disturbance; the latter events are more likely to occur when the growth is situated at the lower end of the common bile-duct.

CLINICAL PICTURE.

The onset is usually insidious, and generally the first thing noticed is jaundice, to which the patient's attention may be called by his friends.

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* Lecène and Pagniez: Archiv. général. de Méd., 1901, p. 176.

† Fütterer, G.: Chicago Reporter, vol. xii, April, 1897.

In some instances there may be an acute onset of gastro-intestinal symptoms, followed by jaundice and suggesting ordinary catarrhal jaundice. Occasionally somewhat vague dyspeptic symptoms exist for some little time before the appearance of jaundice. In a few cases the sudden onset of pain followed by jaundice imitates the impaction of a gall-stone in the common duct.

Symptoms.—Jaundice is necessarily always present; it steadily progresses, and eventually becomes dark-green or black. In only one case, the first recorded, has jaundice been absent. (Durand-Fardel.*) There are gastro-intestinal symptoms, furred tongue, foul breath, dyspepsia, vomiting, and constipation, which may alternate with diarrhœa. The fæces are pale and devoid of bile-pigment. There may be distaste for fatty, or indeed for all food; when jaundice is advanced, there may be small gastro-intestinal hæmorrhagẻs from cholæmia. The symptoms are largely those of jaundice combined with progressive loss of strength and flesh. Attacks of biliary colic, which may be due to cholelithiasis, but are usually independent of the presence of calculi, are met with occasionally; this pseudo-gall-stone colic may be explained as due to spasm of the ducts set up by the irritation of the growth, and is sometimes seen in malignant disease of the head of the pancreas.

Pain of a dull character may be present in the right hypochondrium, but is occasionally present on both sides.

Pain is sometimes felt in the epigastrium, as in carcinoma of the head of the pancreas, and may then be due to invasion of the head of the pancreas by a growth starting in the lower end of the common bile-duct. This form of pain is not, as a rule, a marked symptom.

Itching of the skin usually occurs when jaundice is well marked, but occasionally it precedes the appearance of manifest icterus, though it is probably then the earliest result of the bile entering the circulation. Again, in some instances, there may be little or no itching, even when the jaundice is very deep.

The gall-bladder tends to become distended as a result of backward pressure, and is palpable in about half the cases as a uniform smooth tumor. The smooth surface is important in distinguishing it from primary carcinoma of the gall-bladder.

The gall-bladder is probably always enlarged, except when the growth involves the common hepatic or hepatic ducts, but it is not necessarily palpable during life. The condition of the liver varies considerably: sometimes it is enlarged and smooth from distension with bile; at other times, though large, it is concealed by tympanitic, or more rarely by ascitic, distension, while it may be of the normal size. Secondary growths are very seldom felt during life; in fact, there is hardly time for generalisation to occur widely, as the disease kills comparatively rapidly by cholæmia. When secondary growths are present, they may set up ascites by pressing on the portal vein or by irritating the peritoneum. Ascites is not very frequently a prominent feature. It is, however, present in about half the cases examined after death (Devic and Gallavardin [*]), and is often slight in amount and not of any clinical import.

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* Durand-Fardel: Archiv. gén. de Méd., 1840, p. 147.

The spleen is rarely palpable. In Devic and Gallavardin's 55 cases it was noted as palpable in 8.

The urine is diminished in quantity and deeply bile-stained. Occasionally albuminuria is recorded, but, as a rule, there is no albumin or sugar. Casts are present without albuminuria.

The progressive jaundice usually lasts about five or six months. The patient's condition is one of depression, the temperature being subnormal, unless some secondary infection occurs. Xanthopsia, when everything the patient sees has a yellow tinge, is sometimes present. The usual duration of jaundice—five to six months—is not sufficiently long to allow of the development of xanthelasma, which is usually associated with jaundice of considerable standing.[†]

Pye Smith,[‡] however, has briefly recorded xanthelasma in a case of primary carcinoma of the common duct. The symptoms of biliary toxæmia precede death, which may be from exhaustion, coma, or delirium. The biliary toxæmia is due to two factors: (i) a general poisoning of the blood by toxines manufactured in the alimentary canal and normally stopped, and either destroyed in the liver or excreted into the bile—this is due to a failure of the protective or detoxicating function of the liver—and (ii) to the action of bilirubin on the tissues. Hæmorrhages into the skin and severe itching, when they occur, are due to this toxic condition of the blood. In very rare instances death may be due to peritonitis set up by perforation of the gall-bladder. In a case recorded by May [§] there were two gall-stones in the perforated gall-bladder, while in Coats' and Finlayson's [‖] case there was no history or sign of cholelithiasis.

Death may in very rare instances be due to hæmorrhage taking place around the growth. This occurred spontaneously in one case which I examined after death, and is a source of danger in cases where any operative measures—such as cholecystenterostomy—are undertaken.

Complications.—Besides hæmorrhage around the growth and rupture of the gall-bladder, suppurative cholangitis with or without multiple miliary abscesses has been known to occur. This is more likely to supervene when the growth is near the termination of the common bile-duct. As in cholelithiasis, infective endocarditis has been known to develop, the conditions of deep jaundice being favourable for infection. Thrombosis of the portal vein was found in Bourgeret and Cossy's [**] case.

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[*] Devic and Gallavardin: Rev. de Méd., Aug., 1901, p. 676.

[†] *Vide* a list of 23 cases of xanthelasma associated with jaundice tabulated in the Transactions of the Pathological Society, 1882, p. 381, vol. xxxiii.

[‡] Pye Smith: Trans. Path. Soc., vol. xxviii, p. 243.

[§] May: München. med. Wochen., Bd. xxxix, S. 590, 1892.

[‖] Coats and Finlayson: Glasgow Med. Journ., vol. xxxiv, p. 84, Aug., 1890.

[**] Bourgeret and Cossy: Bull. Soc. Anat., 1873, p. 347.

DIAGNOSIS.

The painless onset, the steadily progressive character of the obstructive jaundice, eventually becoming dark green, the age of the patient,—viz., between fifty and sixty,—and the absence of definite proof of any other cause are the factors which suggest malignant disease of the bile-ducts. But as it imitates persistent obstructive jaundice due to other conditions, it will be advisable to consider the differential diagnosis between them seriatim.

Primary carcinoma of the head of the pancreas, though it does not so surely compress or obstruct the common bile-duct, often produces progressive jaundice. It is only when jaundice is present that the question of the differential diagnosis from primary malignant disease of the ducts arises. In addition to jaundice, both these conditions may or may not show dilatation of the gall-bladder during life, so this point is of no use in the diagnosis. As regards pain, that of pancreatic carcinoma is epigastric, but from extension of the growth to the bile-ducts it may trespass into the hypogastric region. Enlargement of the liver is generally absent in both, though it has been thought to be more frequently seen in bile-duct carcinoma, and secondary growths in the liver are perhaps more often present in pancreatic cancer. In pancreatic disease the primary tumor is seldom, while in carcinoma of the bile-ducts it is almost never, palpable. In both cases the cachexia is rapid,—perhaps more so in cancer of the pancreas,—and death results from cholæmia. A certain amount of variation with regard to the condition of the liver and gall-bladder, and in the site of pain, may occur in both. In short, a diagnosis between the two cannot, on the foregoing grounds, be made with any approach to confidence, and since pancreatic carcinoma is the commoner, it would, on the score of probabilities, be diagnosed whenever their common symptoms are presented. When carcinoma of the lower end of the bile-duct spreads into the pancreas, it may compress Wirsung's duct as well, and so lead to practically the same morbid condition as primary carcinoma of the head of the pancreas compressing the bile-duct.

When, however, the bile-duct alone is compressed, the interference with digestion and assimilation theoretically should be much less than when both it and the pancreatic duct are obstructed, as generally must occur in pancreatic carcinoma. Attention has been called to the presence of large quantities of solid fat * in the motions in obstruction of the pancreatic duct, and to a special alteration † of the fæces, depending on the absence of the pancreatic juice from the intestine. In cases of obstruction of both ducts the fæces sometimes show a great excess of fat over that met with when the bile-duct alone is obstructed, but whether those features are sufficiently constant to be characteristic remains to be proved by more systematic examinations and is worth investigation.

At present it must be admitted that a certain diagnosis between primary carcinoma of the bile-ducts and that of the head of the pancreas cannot be made. By means of his "pancreatic reaction" Cammidge* is able, by examination of the urine, to distinguish cases in which the pancreas is the site of growth, etc., from those in which it is unaffected. In a recent case of carcinoma of the lower end of the common hepatic duct under my care this reaction was negative. The same is probably true as regards differential diagnosis between primary carcinoma of the common bile-duct and carcinoma of the ampulla of Vater. This point is considered more in detail on page 701.

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* Harley, G.: Path. Trans., vol. xiii, p. 118. Harley, V.: Path. Journal, vol. iii, p. 246.

† Walker, T. J.: Medico-Chirurg. Trans., vol. lxxii, p. 257.

Gall-stones, impacted or lying in the common bile-duct, should be indicated by a distinct history of biliary colic immediately preceding the onset of jaundice. But in a patient whose cystic and common bile-ducts are already dilated by the passage of gall-stones, impaction of a calculus may occur, especially near the duodenum, without any satisfactory history of its occurrence. In about a third of the cases of carcinoma of the bile-ducts calculi are found postmortem in the gall-bladder, and in a small proportion of these biliary colic has occurred in life. Conversely, pseudo-gall-stone colic may possibly occur in cases of malignant disease affecting the bile-ducts in the absence of any calculi. When biliary colic immediately precedes the development of icterus, the diagnosis of cholelithiasis is more probable, but since impaction of the gall-stones in the common duct may take place without a characteristic history, it is desirable to consider any further points which bear on the diagnosis of gall-stone obstruction from that due to bile-duct carcinoma. The duration of calculous jaundice is very much longer than that of carcinoma of the bile-ducts, and death, when it occurs, is usually due to some complication, such as suppurative cholangitis, rather than to cholæmia. This difference in the course of the two affections is correlated with a difference in the nature of the obstruction in each case. In malignant disease the obstruction becomes more marked, and in nearly all cases absolute as time goes on, whereas exactly the reverse holds good with gall-stone impaction; the obstruction is complete at first, but subsequently, from the constant pressure exerted from within by the calculus on the wall of the bile-duct, from inflammation, and to some extent from extension of the dilatation of the ducts above the obstruction, the walls of the duct become somewhat separated from the calculus, and the obstruction becomes partial or so slight that eventually the jaundice may almost disappear. In gall-stone obstruction of the common duct periodic attacks of intermittent hepatic fever usually occur (*vide* p. 750) which are quite characteristic of this condition.

The course and duration of the diseases, if uninterrupted by surgical treatment, are therefore sufficiently distinct to enable a differential diagnosis to be made, though this may not be possible in the earlier stages.

Courvoisier's law, namely, that in calculous obstruction of the common bile-duct the gall-bladder is not enlarged, while in obstruction of that duct by new-growth the gall-bladder forms a palpable tumor, should always be borne in mind. But the gall-bladder need not be enlarged in all cases of carcinoma of the bile-ducts. Thus when carcinoma arises in the common hepatic or in either of the hepatic ducts, the gall-bladder is not enlarged, and there may be difficulty in diagnosing the condition from impacted calculus in the common duct. But in a doubtful case enlargement of the gall-bladder is in favour of the obstruction being due to malignant disease and not to gall-stones in the common duct. The following points, then, would be in favour of cholelithiasis: The history of colic immediately preceding the onset of jaundice; intermittent hepatic fever; the chronic nature of the illness; the absence of enlargement of the gall-bladder, and the fact that although of considerable duration, the jaundice is not very deep or progressive.

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* Cammidge, P. J.: Lancet, 1904, vol. i.

In **primary malignant disease of the gall-bladder,** so long as the growth remains limited to the gall-bladder and there is no pressure on the hepatic or common ducts, jaundice is absent, and there is little resemblance between this disease and primary carcinoma of the ducts. The jaundice is, therefore, no essential part of the disease, and is due either to extension of the primary growth or to pressure exerted by secondary growths on the bile-ducts. It occurs in the course of more than half the cases—according to Musser, in 69 per cent., which is, curiously enough, also the proportion in which gall-stones were present in his 100 cases of carcinoma of the gall-bladder. When jaundice, due to obstruction of the duct, has supervened, the case is for all practical purposes one of malignant disease both of the gall-bladder and of the bile-ducts. This condition is even less amenable to palliative operative treatment than malignant disease of the common bile-duct; for in the latter condition the operation of cholecystenterostomy can be resorted to for the relief of cholæmia with a fair prospect of success. In carcinoma of the gall-bladder there may be a tumor in its situation, which is knobby or irregular, and is not so large as the smooth, dilated gall-bladder frequently met with in carcinoma of the bile-ducts or of the head of the pancreas. In addition to the history, the very frequent association (80–95 per cent.) of gall-stones with carcinoma of the gall-bladder should be kept in mind.

In **malignant disease of the liver,** whether primary or secondary, with jaundice, the history of the case and the facts that the liver is considerably enlarged and manifestly infiltrated with growth and that the jaundice is not so extreme, or, as a rule, of such long duration, will serve to differentiate it from primary carcinoma of the ducts.

From **hypertrophic biliary cirrhosis** there will seldom be any real difficulty in diagnosis. In some exceptional cases of bile-duct carcinoma the spleen is enlarged, but not to the same extent as in biliary cirrhosis. The latter disease occurs in younger persons, runs a chronic course, measured by years and not by months, and presents much greater enlargement of the liver and spleen.

Catarrhal jaundice is usually ushered in by vomiting and diarrhœa, while the onset of jaundice due to malignant stricture of the bile-duct is usually unobtrusive and unaccompanied by signs of gastro-intestinal catarrh. But the course of the two is so different—the one passing almost spontaneously away in a few weeks, the other getting progressively worse—that even if at first there be difficulty in determining which is the cause at work, little doubt remains after a few weeks have gone by.

There are a number of other causes which may sometimes give rise to chronic jaundice of varying degree, such as secondary malignant disease in the portal fissure, growths, tumors, or hydatid cysts in connexion with the liver, inflammatory adhesions, or even possibly gummata implicating the ducts, aneurysms of the hepatic artery or of the abdominal aorta—in short, most of the tumors and many of the morbid conditions to be met with in the abdominal cavity (*vide* p. 541).

But the question of diagnosis will seldom arise between them and primary malignant disease of the ducts, inasmuch as there will generally be, either in the history or in the physical signs and symptoms, a clue to the nature of the disease.

TREATMENT.

The treatment of cases thought to be malignant disease of the bile-ducts has usually been confined to relieving symptoms and alleviating pain and distress, and an attempt to prevent putrefactive changes in the intestines by antiseptics and by an appropriate diet. The palliative and symptomatic treatment is that of obstructive jaundice (*vide* p. 535). Pain may require morphia; pruritus, bathing with carbolic acid lotion (1 : 40) or the application of a dusting-powder of starch (1 oz.), oxide of zinc (℥ss), and camphor (ʒiss) (McCall Anderson); antipyrin internally, or hypodermic injections of pilocarpine. Chloride of calcium may be given both for pruritus and to prevent hæmorrhages. Intestinal putrefaction may be combated by minute doses of calomel ($\frac{1}{40}$–$\frac{1}{20}$ gr.) and by preventing constipation by blue pill and salines. Cholæmia may be obviated temporarily by intravenous or better by subcutaneous transfusion if it is thought to be worth while.

Surgical interference has not been much in vogue, presumably because radical measures are very difficult and the disease is necessarily fatal. Though it cannot be more than palliative, the operation of putting the gall-bladder into communication with the small intestine—cholecystenterostomy—will, in favourable cases,—*i. e.*, where the obstruction is limited to the common bile-duct,—prevent the bile being dammed up in the liver and absorbed by the lymphatics into the general circulation. Jaundice and cholæmia, with their attendant symptoms, may thus be obviated, and the patient's general condition greatly improved. As already mentioned, death is likely to occur in complete biliary obstruction from cholæmia, and if this is prevented, life may be greatly prolonged.[*]

In a case of biliary obstruction due to what turned out to be malignant disease of the pancreas Reclus[†] performed cholecystenterostomy with the remarkably successful result that the patient experienced great relief and survived the operation for twenty-one months, eventually dying with numerous secondary growths.

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[*] For the surgical treatment of carcinoma of the bile-ducts see Terrier ain Auvray: Chirurgie du foie et des Voies biliaires, 1900; Schwartz: Chirurgie du foie, 1900; Mayo Robson: Diseases of the Gall-bladder, 1904.

[†] Reclus: Sem Méd., 1893, p. 569.

Curative Surgical Measures.—The resection of a growth from the bile-duct with union of the two divided ends is the ideal operation, but it is extremely difficult. In the only recorded case of this kind—Kehr's[*]—in which a carcinoma at the junction of the common hepatic, cystic, and common bile-ducts was resected, it was impossible to unite the cut ends of the common bile-duct and hepatic duct, so the latter was implanted into the duodenum, the cut end of the common bile-duct being ligatured. This case recovered from the operation, and it may, therefore, be expected that further successes will be obtained. Reference to removal of growths in the region of the diverticulum of Vater is made on page 702.

Malignant disease of the cystic duct has been removed (Warren[†]), but this operation is more allied to excision of the gall-bladder and is not so beset with difficulties as resection of part of the hepatic or common bile-ducts.

CARCINOMA OF THE AMPULLA OF VATER.

The common bile-duct, before opening into the duodenum, joins with the main pancreatic duct; this common portion is called the ampulla or diverticulum of Vater. Normally the mucous membrane of the ampulla contains glands (Pilliet[‡]) and is thrown into folds. It thus appears rougher than the inside of the common bile-duct, but it is not dilated except under very definite pathological conditions, such as impaction of a gall-stone. Carcinoma may start in the mucous membrane of the ampulla, or may spread to it from the lower end of the bile-duct or from the termination of the pancreatic duct.

Busson,[§] in 1890, collected 11 cases of carcinoma of the diverticulum Vateri, and in 1896 Vincent Georges,[‖] a pupil of Hanot's, collected 9 more. Hanot[**] added another later in the same year. Of these 21 cases only about half a dozen are genuine examples of carcinoma of the ampulla of Vater, the others being either carcinoma of the lower end of the bile-duct or carcinoma of the duodenal surface of the biliary papilla.

I have collected 16 cases,[††] 14 of them since the beginning of 1896, which appear to be undoubted examples of carcinoma arising in the mucous membrane lining the diverticulum Vateri.

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[*] Kehr: München. med. Wochen., 1903, S. 101.

[†] Warren: Boston Med. and Surg. Journ., March 15, 1900, p. 276.

[‡] Pilliet: Compt. rend. Soc. Biolog. Paris, 1894, p. 549.

[§] Busson: Thèse de Paris, 1890.

[‖] Vincent Georges: Thèse de Paris, 1896, No. 404.

[**] Hanot: Archiv. général. de Méd., vol. clxxviii, p. 547. Previous cases recorded by Hanot are given in Vincent Georges' thesis.

[††] Durand-Fardell: La Presse Médical, 1896. Vincent Georges: Thèse de Paris, 1896, No. 404. Rendu: Soc. Méd. des Hôp., May 1, 1896. Hanot: Archiv. général. de Méd., t. clxxviii, p. 547. Pilliet: Bull. Soc. Anat. Paris, 1889, p. 509. Dominici: Bull. Soc. Anat. Paris, 1896, p. 709. Maury: Soc. Méd. des Hôp., May 9, 1902, p. 433. Cornil and Chevassu: Bull. Soc. Anat. Paris, 1903, p. 151. May: München. med. Wochen., Aug. 16, 1892. Scheuer: Berlin. klin. Wochen., Feb. 17, 1902. Halsted: Johns Hopkins Hosp. Bull., No. 103, Jan., 1900. Pratt and Fulton: Boston Medical and Surgical Journ., June, 1900, p. 599. De Havilland Hall: Lancet, 1902, vol. i, p. 1102. Klotz: Montreal Med. Journ., vol. xxxiii, p. 477, 1904. Rolleston: Lancet, 1901, vol. i, and one from St. George's Hospital, *vide* p. 702.

Hanot * regarded carcinoma of the ampulla of Vater as distinct from carcinoma of the lower end of the bile-duct, or, as it is called, juxta-ampullary carcinoma of the common bile-duct. He laid stress on the fact that the growth is limited to the ampulla of Vater, and does not arise in the common bile-duct or in the duodenum. He spoke of the condition as *cancer du pylore pancréatico-biliaire*. The diagram represents his views. It must be admitted, however, that the parts are so small that it may be very difficult or even impossible to distinguish the form arising in the termination of the bile-duct (*vide* 1, in diagram), from that arising from the lining of the ampulla (*vide* 4, in diagram), away from the opening of the common bile-duct.

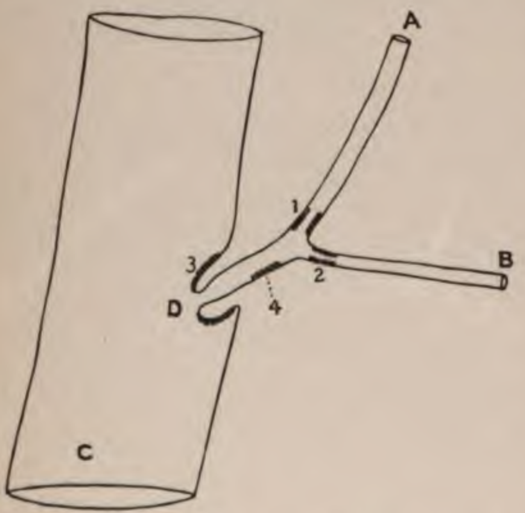

FIG. 91.—DIAGRAM OF THE AMPULLA VATERI, SHOWING THE VARIOUS SITUATIONS WHERE CARCINOMA MAY ARISE IN RELATION WITH IT AND IN ITS NEIGHBOURHOOD.

A, Common bile-duct. B, Wirsung's duct. C, Duodenum. D, Biliary papilla. 1, Carcinoma of the termination of the common bile-duct. 2, Carcinoma of the termination of Wirsung's duct. 3, Carcinoma of the duodenal surface of the biliary papilla. 4, Carcinoma of the ampulla Vateri itself.†

Primary carcinoma of the ampulla Vateri, or, as it might more conveniently be called, the choledochopancreatic duct, must be also distinguished from primary carcinoma attacking the mucous membrane covering the duodenal surface of the biliary papilla. Specimens of this form of duodenal carcinoma are to be found in the museums of St. Bartholomew's, Guy's, and St. Thomas' Hospitals. This lesion seems to be especially prone to lead to infective cholangitis and intra-hepatic suppuration. Carcinoma of the ampulla of Vater must thus be distinguished from carcinoma (1) of the termination of the common bile-duct; (2) of the termination of Wirsung's duct; and (3) of the duodenal surface of the biliary papilla. The accompanying diagram illustrates these distinctions. Confusion may also occur between carcinoma of the head of the pancreas and primary carcinoma of the ampulla Vateri. Histologically they differ: carcinoma of the pancreas is spheroidal-celled, while carcinoma of the diverticulum Vateri is columnar-celled.

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* Hanot: Archiv. gén. de Méd., vol. clxxviii, Nov., 1896, p. 547.

† For this figure, which illustrated a paper of mine in the Lancet of Feb. 17, 1901, I am indebted to the proprietors of that journal.

Pic * regarded carcinoma of the ampulla as an aberrant form of pancreatic carcinoma corresponding apparently with the excretory type (columnar-celled) of the pancreatic growth described by Bard and Pic.† Luzzato ‡ has described two cases of carcinoma of the Vaterian region arising from the excretory ducts of the pancreas. This is tantamount to considering it to be carcinoma of the end of the pancreatic duct.

Morbid Anatomy.—The growth begins as a thickening of the mucous membrane of the ampulla and infiltrates its muscular walls. It may form a villous or polypoid growth, and may then project through the orifice of the biliary papilla, which is dilated or ulcerated, into the duodenum. The growth is white, as a rule, but may be of a pinkish-white colour when projecting into the duodenum. It is always comparatively small, and rarely shows any naked-eye evidence of ulceration. It is probable, from the histological accounts given, that some of the cases described as carcinoma of the diverticulum of Vater were simple papillomatous, and not malignant, growths. A growth in this situation, whether innocent or malignant, would rapidly give rise to jaundice and to cholæmia. Secondary growths are seldom found in the recorded cases; this may be due to the growth being an innocent papilloma, or, if a carcinoma, to its killing the patient from cholæmia before there has been time for secondary growths to occur. If cholæmia is prevented by establishing a biliary fistula, as in case on p. 702, life may be prolonged and secondary growths develop.

Histologically it is, like primary carcinoma of the bile-ducts, practically always a columnar-celled carcinoma. But from its position its pathological effects are not absolutely identical with those of carcinoma of the bile-ducts. A growth in the ampulla of Vater tends to obstruct the orifice of Wirsung's duct and thus to produce dilatation of the intrapancreatic ducts and chronic interstitial pancreatitis. This is well shown in the cases described on pages 701 and 702. It is, of course, possible, however, for carcinoma of the lower end of the common bile-duct to extend into the ampulla and thus obstruct the orifice of Wirsung's duct. When, from obstruction to Wirsung's duct or from ascending infection, chronic interstitial pancreatitis results, it might have been expected that diabetes would occur. This, however, does not appear to have been met with. The explanation of this has been given by Opie,§ who has shown that obstruction of the duct is very seldom followed by such intimate fibrosis of the pancreas as to destroy the areas of cells called the islands of Langerhans. These structures almost certainly provide the internal secretion of the pancreas, which prevents glycosuria. Hence so long as they are intact diabetes does not develop.

If carcinoma arising in the ampulla of Vater involved the mucosa and walls of the orifice of the biliary papilla, it might, provided the growth did not involve the orifice of Wirsung's duct, convert the common bile-duct and Wirsung's duct into a common and closed channel. The entrance of bile into the pancreatic duct might then occur and set up hæmorrhagic pancreatitis. This production of hæmorrhagic pancreatitis by a small calculus impacted in the biliary papilla has been proved by Halsted and Opie.*

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* Pic: Rev. de Méd., 1895, p. 71.

† Bard and Pic: Rev. de Méd., 1888, p. 394.

‡ Luzzato: La Clinica Medica Italiana, 1902, p. 282.

§ Opie, E. L.: Jour. Exper. Med., vol. v, p. 397, 1901. Diseases of Pancreas, p. 178 1903.

An ascending infection of the bile-ducts may induce suppurative cholangitis and multiple hepatic abscesses; this accident is more likely to occur than in primary carcinoma of the bile-ducts.

In a case recorded by Pratt and Fulton,† the pus from multiple abscesses in the liver gave a pure culture of the Bacillus aërogenes capsulatus, but there was no gas-formation.

Etiology.—The male sex are much more often affected than the female sex, thus differing from malignant primary disease of the gall-bladder and resembling the sex incidence in primary malignant disease of the larger bile-ducts. In 16 cases 13 were males and 3 females.

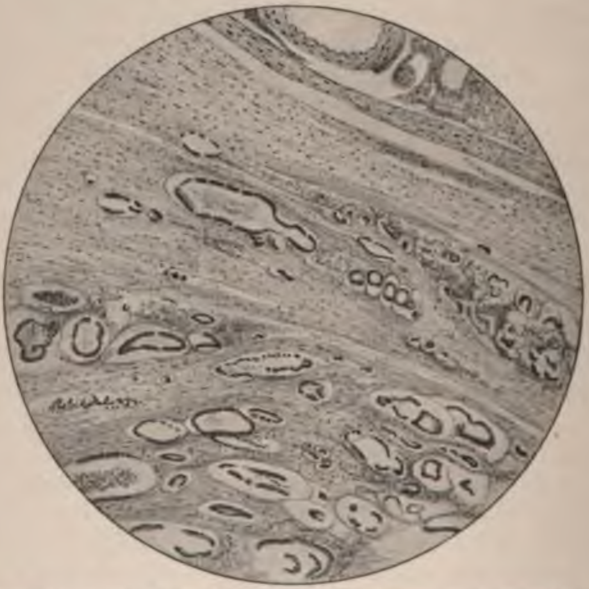

FIG. 92.—CARCINOMA OF THE AMPULLA OF VATER INVADING THE MUSCULAR WALLS OF THE DUCT AND DUODENUM. IT IS A COLUMNAR-CELLED CARCINOMA.

It is a disease of advanced life. In 16 cases the average age was 55.6 years, being 55.6 years in the 12 males, and 55.6 years in the 3 females. The extremes were 34 and 81 years.

There is no relation between gall-stones and this form of malignant disease of the biliary system; in only 2 out of 16 cases were calculi present. This is rather remarkable, since gall-stones are not infrequently found in the diverticulum Vateri, and may remain there for very considerable periods, so that it might naturally have been assumed, on the analogy of the gall-bladder, that their irritation would give rise to carcinoma.

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* Halsted and Opie: Johns Hopkins Hospital Bulletin, vol. xii, Nos. 121, 122, 123. April, May, June, 1901.

† Pratt and Fulton: Boston Med. and Surg. Jour., June 7, 1900, p. 599.

The **symptoms, signs, and diagnosis** of carcinoma of the ampulla are, in the main, the same as those in cancer of the common bile-duct (the reader is referred to p. 691). There are only a few points of difference requiring attention as bearing on the diagnosis between the two conditions, which must be regarded as a very difficult or even impossible problem:

(i) Jaundice is said to be often intermittent, the fæces becoming bile-stained and the icteric tint of the skin diminishing or even passing off in the earlier stages when the obstruction is possibly valvular, or partly due to spasm of the duct set up by the irritation of the growth. In this connexion it may again be pointed out that confusion is apt to arise in recorded cases between carcinoma of the ampulla and of carcinoma of the duodenal surface of the papilla, in which jaundice is by no means constant. (ii) Intermittent hepatic fever and suppurative cholangitis are apt to occur. (iii) Diarrhœa is more often seen than in carcinoma of the ducts, where constipation is the rule. Attacks of diarrhœa may alternate with periods of obstinate constipation. The clinical manifestations of the disease are illustrated by the following cases:

Carcinoma of the Ampulla of Vater. Dilated Bile and Pancreatic Ducts. Hæmorrhage into Pancreatic Duct.—A man aged sixty-six was admitted into St. George's Hospital under my care on July 22, 1900, with jaundice, pruritus, weakness, and wasting. He had never had any severe illness, denied alcoholic excess and syphilis. Ten weeks previously he had been quite well; jaundice then appeared quite painlessly. A month later he began to waste, got weaker, and became drowsy, and two weeks later the skin began to itch. When examined on admission he was deeply jaundiced, the skin showing the effects of scratching; the liver was enlarged, reaching to fourth rib above and two and one-half fingerbreadths below in the right nipple line. It was quite smooth; the gall-bladder could be indistinctly felt; the spleen could not be made out. The abdomen was somewhat distended, but there was no evidence of ascites. There was tenderness at a spot over the eleventh and twelfth ribs in the right hypochondrium. Per rectum nothing abnormal, except an hypertrophied prostate, could be felt. The urine contained albumin, bile-pigments, and bile acids, but no sugar. A tentative diagnosis of malignant disease of the head of the pancreas was made. On July 25th he had diarrhœa, on July 26th he vomited, had a rigor, and the temperature fell to 96°; pulse 96, small. Respirations were 36 and the abdomen moved well. The liver seemed larger than on admission. The freedom with which the abdomen moved made it appear unlikely that perforation into the peritoneum had taken place; suppuration around the gall-bladder was thought of, but his condition was so bad that ⅓ grain of morphia was given hypodermically to relieve his pain and distress. He died eighteen hours after the onset of acute symptoms.

The autopsy showed a small, hard growth arising from the mucous membrane of the cavity common to the openings of the common bile-duct and the pancreatic duct, entirely inside the biliary papilla, and not visible from the duodenum. The growth blocked the pancreatic and common bile-ducts. The common bile-duct was as big as one's thumb and contained dark bile and mucus; when opened and the finger introduced in a downward direction, it was found to end blindly, like a test-tube. The hepatic ducts and the ducts in the left lobe of the liver were widely dilated; except the main right hepatic duct, the bile-ducts in the right lobe were but little dilated. The cystic duct and gall-bladder were greatly dilated; no calculi were found in the gall-bladder or in the bile-ducts. The liver (4 pounds) was smooth and of a deep green colour. Wirsung's duct was tortuous, dilated throughout its entire length, while near the head of the pancreas it formed a cyst into which recent hæmorrhage had taken place. It is probable that the terminal acute symptoms depended on this hæmorrhage. Towards the tail of the pancreas the duct contained dark fluid, probably altered blood of older date. The pancreas was adherent to the posterior wall of the stomach by old adhesions, evidently the result of former inflammation. No calculi were found in the ducts of the pancreas. The pancreas itself was greatly fibrosed and hard. No secondary growths were found in any part of the body. The abdomen contained two pints of bile-stained fluid. The stomach and intestines showed signs of recent catarrhal inflammation. *Kidneys* (6 ounces each) showed senile change and a few cysts. Heart (11 ounces) was normal for the time of life. The lungs were emphysematous and showed hypostatic congestion.

Microscopically the growth was a columnar-celled carcinoma and invaded the muscular coat, lying under the floor of the ampulla of Vater (*vide* Fig. 92). The pancreas showed extensive fibrosis, some recent small-cell infiltration, dilatation of the ducts, which contained minute calculous masses, and widespread atrophy of the glandular tissue of the pancreas. The islands of Langerhans were, however, intact; this may be correlated with the absence of glycosuria.*

Carcinoma of the Ampulla Vateri Imitating Cholelithiasis.—A woman aged fifty-two was attacked six and a half months before death with colic, shivering, diarrhœa, vomiting, and distension of the abdomen. The pain lasted for two weeks and was succeeded by jaundice. She had several similar attacks resembling biliary colic, and when admitted to St. George's Hospital, under the care of Dr. Cavafy, on March 30, 1892, had lost three stone in weight. She was deeply jaundiced and complained of abdominal tenderness, itching of the skin, and weakness. Grating was felt in the region of the gall-bladder. Cholecystotomy was performed, but no calculi were found. At the operation there was ascites. Before death nodules of growth appeared in the skin around the fistula leading into the gall-bladder.

At the autopsy, which I performed, a growth was found projecting from the gaping lips of the biliary papilla; it arose inside the ampulla of Vater and completely blocked the common bile-duct; the duct of Wirsung was obstructed and presented a cystic dilatation as large as a hen's egg near the tail of the pancreas, which was adherent to the fundus of the stomach.

There were a number of secondary growths in the liver, which was small and deeply bile-stained. There was no cirrhosis microscopically, but numerous masses of inspissated bile in the minute bile-ducts. Microscopically the growth was a columnar-celled carcinoma.

The **treatment** of carcinoma of the ampulla has so far, with the exception of Halsted's † and Mayo's cases, been palliative and confined to relief of the symptoms and on the same lines as in carcinoma of the bile-ducts.

Halsted successfully performed a radical operation consisting in the wide removal of a primary carcinoma of the duodenal papilla and diverticulum Vateri in a woman aged sixty. The common bile-duct and pancreatic ducts were engrafted into the duodenum; three months later the cystic duct was engrafted into the duodenum to relieve the biliary obstruction which had persisted. Death occurred within a year of the first operation from recurrent carcinoma in the head of the pancreas and duodenum, which had obstructed the openings of the common and cystic ducts into the duodenum. In a somewhat similar case Mayo ‡ removed a carcinoma of the terminal part of the common bile-duct by the duodenal route; it recurred in eighteen months' time. The result of this brilliant and formidable surgical procedure is disappointing.

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* This case was reported in the Lancet, 1901, vol. i, p. 467.

† Halsted: Johns Hopkins Hospital Bulletin, No. 103, Jan., 1900.

‡ Mayo: Boston Medical and Surgical Journ., vol. cxlviii, p. 545, 1903.

CHOLELITHIASIS.

CAUSES OF CHOLELITHIASIS.

The formation of gall-stones, whether in the ducts or in the gall-bladder, may be considered under the following two heads—(i) Immediate or exciting causes. (ii) Disposing factors.

IMMEDIATE OR EXCITING FACTORS.

The immediate cause of the production of calculi is a mild form of catarrhal inflammation of the mucous membrane lining the ducts and gall-bladder. Catarrhal inflammation of the bile-ducts leads to an albuminous exudation which, as shown by experimental addition of egg-albumin to bile, precipitates bilirubin in chemical combination with calcium * as bilirubin-calcium calculi. This is the only form of calculus actually produced in the bile-ducts, though under conditions such as impaction of a gall-stone in the common duct the formation of additional calculous material containing cholesterin, as well as bilirubin-calcium, takes place.

Simple stagnation and inspissation of bile do not lead to the precipitation of bilirubin-calcium or to the formation of bilihumin, which is constantly found in these bilirubin-calcium calculi. Something more than inspissation—viz., catarrhal inflammation—is necessary for the formation of these calculi.

In catarrhal inflammation of the mucous membrane of the gall-bladder there is an abnormal formation and secretion of cholesterin by the mucous cells and glands in its walls. This excessive and pathological production of cholesterin is responsible for the formation of cholesterin calculi. This differs from the ancient conception that cholelithiasis was due to a mere precipitation of the cholesterin normally present in bile, brought about by a change in the characters of the bile, such as concentration or alteration in its chemical properties or reaction.

Inflammation of the gall-bladder leads to a perverted metabolism inside the mucus-secreting cells in its walls, resulting in the formation of cholesterin inside these cells. Evidence of this can be seen microscopically in the presence of myelin bodies inside the cells. It was formerly thought that the cholesterin formed elsewhere, and especially in the central nervous system, was picked up from the blood and excreted into the gall-bladder, but there is no evidence to support this, since administration of cholesterin to animals under the skin or by the mouth does not increase the amount of cholesterin in the bile.

It will be noticed that the results of catarrh in the small bile-ducts

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* Naunyn: Cholelithiasis, p. 20. Translated by New Sydenham Soc., 1896.

and in the gall-bladder differ both in the mechanism and in the nature of the calculi produced. As the result of catarrh of the small intra-hepatic ducts there is a precipitation of bilirubin-calcium, while catarrh of the gall-bladder leads, by a perverted metabolism of the mucous membrane, to a pathological formation of cholesterin analogous to that seen in certain cysts, such as hydroceles, ovarian, etc.

The catarrh of the ducts and gall-bladder may be spoken of as lithogenic. If the catarrh starts in the ducts, the small calculi of bilirubinate of calcium may possibly find their way into the gall-bladder and there form the nucleus of cholesterin calculi formed as the result of an extension of the inflammation to the gall-bladder. Acute suppurative inflammations of the ducts and gall-bladder do not lead to the formation of calculi. This would appear to depend on the fact that destruction of the mucous cells necessarily prevents the formation of cholesterin. As catarrhal inflammation is the essential antecedent of cholelithiasis, it will be necessary to consider what are the exciting and disposing causes of catarrhal cholecystitis and cholangitis.

The exciting causes are infection with micro-organisms and possibly the action of poisons excreted into the ducts.

The **microbic origin of gall-stones** has attracted very considerable attention since it was first suggested by Galippe* in 1886. Experimentally it has been shown that the production of cholecystitis by the bacillus of typhoid fever and the colon bacillus is followed by cholelithiasis. Non-virulent cultures of streptococci and staphylococci may also give rise to calculus formation; virulent cultures, however, set up intense cholecystitis without any production of calculi. (Mignot.) From Italia's † researches it appears that pure cultures of streptococci or staphylococci may lead to the formation of calculi which are composed only of lime salts; cholesterin may be found when there is an admixture with cultures of the Bacillus coli. Thus experimental work, like clinical observation, shows that cholelithiasis is due to a comparatively mild form of cholecystitis, or, expressed in other words, is produced by an attenuated infection; this depends on the preservation of the cholesterin-producing epithelium in the slighter forms of cholecystitis and its destruction in more acute inflammations of the gall-bladder.

The important micro-organisms in the production of cholelithiasis are: (1) The colon bacillus. (2) The typhoid bacillus.

(1) The most important part in the microbic origin of biliary calculi is usually ascribed to bacilli *belonging to the colon group*. Experimentally Mignot ‡ produced calculi in a guinea-pig as a result of the action of Bacillus coli in the gall-bladder in 1897. The colon bacillus has often been demonstrated inside biliary calculi (Gilbert and Dominici,§ Mignot, etc.); recent calculi especially show the presence of bacilli, while old calculi usually do not, or at best show only the faintly staining shadows of micro-organisms.

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* Galippe: Comp. Rend. de la Soc. biolog. Paris, 1886, p. 116.
† Italia: La Riforma Medica, 1901, ii, 830.
‡ Mignot: Soc. de Chirurg., May 19, 1897.
§ Gilbert and Dominici: Soc. de biolog., June 16, 1894, p. 485.

Chauffard,* who rather opposes the bacterial origin of cholelithiasis, has pointed out that the presence of micro-organisms in a calculus does not necessarily prove that they had any part in its formation, since micro-organisms may invade a calculus from the outside.

It is generally believed that the colon bacillus reaches the gall-bladder by an ascending infection of the common bile-duct from the duodenum. It appears, from bacteriological examination of the duodenum in health, that during fasting the mucous membrane may be sterile and that when micro-organisms are found, they are, so to speak, accidental and derived from the ingesta. (Cushing and Livingood.†) It is, therefore, probable that a catarrhal condition of the duodenum would be necessary to enable an ascending infection to occur. A factor of importance in the production of an ascending infection is more or less stagnation of the bile; otherwise the micro-organisms would be washed out of the ducts by the bile. On the other hand, it is highly probable that the colon reaches the liver by the portal vein and is excreted into the ducts.

(2) *Bacillus Typhosus.*—The causal relationship between typhoid fever and gall-stones was suggested by Bernheim,‡ of Nancy, in 1889, on clinical grounds, viz., the occurrence of biliary colic in patients with typhoid fever who had not previously had any signs of gall-stones. Calculi have often been found in the gall-bladder shortly after typhoid fever in patients who had not previously exhibited any signs of cholelithiasis (Gilbert et Girode,§ Hanot,‖ and others). Dufourt** found a history of enteric in 19 cases of cholelithiasis in which no symptoms of gall-stones had appeared previous to the fever. In 12 of these cases symptoms of gall-stones appeared within six months of the attack of enteric fever.

In 42 cases of gall-stones 13 had had typhoid fever and had not had any signs of cholelithiasis before the fever (Curschmann ††).

In typhoid fever the Bacilli typhosi are almost constantly found in the gall-bladder after death, and, as a rule, without any calculus formation. It is, therefore, probable that the production of calculi depends on cholecystitis and not on the presence of micro-organisms alone. Typhoidal cholecystitis is described elsewhere (*vide* p. 593). The agglutination of typhoid bacilli in the bile has been suggested as a nucleus or starting-point for the formation of calculi (Richardson ‡‡), but this is not supported by experiments outside the body; Cushing§§ added typhoid bacilli to bile and then precipitated them by adding serum from a typhoid patient, but failed to obtain any precipitation of material from the bile.

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* Chauffard: Rev. de Méd., Feb., 1897, p. 81.

† Cushing and Livingood: Johns Hopkins Hosp. Reports, vol. ix, p. 543.

‡ Bernheim: Dict. Encyclop. de Dachambre, Article Ictère, 1889.

§ Gilbert and Girode: C. R. Soc. biolog., 1893, p. 958.

‖ Hanot: Bullet. Méd., Jan. 22, 1896.

** Dufourt: Rev. de Méd., 1893, p. 274.

†† Curschmann: Die Unterleibstyphus, Wien, 1898, p. 355.

‡‡ Richardson, M. W.: The Jour. of Boston Soc. of Med. Science, vol. iii, p. 79, Jan., 1899. Quoted by Cushing.

§§ Cushing, H.: Remarks on Dr. Hunner's Case of Typhoidal Cholecystitis, Johns Hopkins Hosp. Bull., Nos. 101, 102, Aug.-Sept., 1899, p. 163.

Gilbert and Dominici,[*] in 1893, in experimental typhoidal cholecystitis in a rabbit, produced greenish concretions. This was confirmed by Gilbert and Fournier[†] in 1897. The question whether typhoid bacilli reach the gall-bladder by means of the portal vein or directly up the common bile- and cystic ducts has been discussed in the section on the Causation of Cholecystitis (*vide* p. 595). Here it may be said that it is more probable that the bacilli are carried to the liver by the portal vein and then excreted into the bile-ducts and so reach the gall-bladder, than that there is an ascending infection from the duodenum.

Leptothricial Cholelithiasis.—Pearce[‡] has described a case of cholelithiasis in a man aged fifty-nine years which seemed to depend on leptothricial infection. The threads of leptothrix were found in the calculi.

Question of the Production of Cholelithiasis by Toxæmia.—The theoretical production of cholecystitis by toxines, such as abrin, and by bacterial poisons has been referred to elsewhere. It was there stated that Claude's[§] experiments make it probable that cholecystitis may be produced by toxines, but though it might reasonably be expected (Gilbert[‖]), I am not aware that a toxic lithogenic catarrh of the gall-bladder has been produced experimentally. It may, therefore, be concluded that although the production of gall-stones from catarrhal inflammation of the gall-bladder set up by the irritating effects of poisons, without any microbic intervention, is logically possible, it has not been shown to occur in man.

DISPOSING CAUSES.

Factors which Favour the Production of Catarrh of the Gall-bladder and Bile-ducts, and so Dispose to Cholelithiasis.—1. *Stagnation of bile* in the gall-bladder does not of itself lead to the formation of calculi, but it renders infection more easy, since if any micro-organisms get into the bile, they are not removed, but allowed to multiply there and may subsequently set up cholecystitis. Further, in the absence of stagnation, micro-organisms present in the gall-bladder need not set up cholecystitis; this has been shown experimentally by Ehret and Stolz,[**] and is supported by the frequency with which cultures of typhoid bacilli are found in the gall-bladder without any evidence of cholecystitis in fatal cases of typhoid fever.

Experimentally Mignot[††] showed that stagnation of bile in an aseptic gall-bladder does not lead to crystallisation of cholesterin out of the bile, and he believes that absolute stagnation of bile prevents the formation of stratified calculi and is less favourable to cholelithiasis than relative inertia of the gall-bladder.

Sedentary habits, want of exercise, obesity, and diseases which necessitate a quiet and restful life dispose to cholelithiasis. Want of exercise carries with it feeble contractions of the abdominal muscles, and as a result bile is not expelled so frequently or efficiently from the gall-bladder. This explains why gall-stones are rare in outdoor labourers and common in women. The influence of a sedentary life is shown by the occurrence of biliary calculi in pet dogs and by their absence in wild animals. Sitting upright and leaning forwards over a desk keep the fundus of the gall-bladder in a dependent position and prevent, or at any rate interfere, with its being properly emptied. It has, therefore, been considered a disease of literary men, but has also been noticed to develop in prisoners confined in gaol. The recumbent posture in an easy chair, however, is favourable to the flow of bile out of the gall-bladder.

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[*] Gilbert and Dominici: Compt. rend. Soc. biolog., 1893, p. 1033.

[†] Gilbert and Fournier: Ibid., 1897, p. 936.

[‡] Pearce, R. M.: University of Pennsylvania Med. Bull., Aug., 1901, p. 217.

[§] Claude: Bull. Soc. Anat. Paris, June–July, 1896.

[‖] Gilbert: Archiv. général. de Méd., Sept., 1898.

[**] Ehret and Stolz: Berlin. klin. Wochen., 1902, S. 13.

[††] Mignot: Archiv. général. de Méd., Aug.–Sept., 1898.

Tight lacing frequently leads to dilatation of the gall-bladder from the downward displacement of the duodenum straining and kinking the cystic duct, which even under normal conditions requires a spiral valve to keep it open. (Keith.[*]) Further, downward displacement of the right lobe of the liver makes the fundus of the gall-bladder more dependent than in health, and, since the cystic duct is more fixed at the transverse fissure of the liver, tends to produce kinking of the duct. A wandering liver has much the same effect. Nephroptosis, or a floating kidney, on the right side may, by traction on the peritoneum covering the common bile-duct in the lesser omentum, obstruct the outflow of bile from the gall-bladder.

Any cause that interferes with diaphragmatic respiration and therefore with the emptying of the gall-bladder tends to produce stagnation of bile in the gall-bladder. Among the factors exerting this influence are tight lacing, abdominal distension from pregnancy, ascites, abdominal tumors, etc., cardiac and pulmonary disease.

2. *Foreign bodies* are, of course, only exceptionally found in the gall-bladder. Aseptic foreign bodies do not give rise to the formation of gall-stones; this has been shown experimentally by Mignot. If, however, cotton-wool impregnated with colon bacilli is introduced into the gall-bladder, calculi are formed. Calculi have been found to contain pins (Nauche,[†] Carless [‡]), pieces of hydatid membrane, the ova of bilharzia (Gautrelet [§]), and round worms (Lobstein). Round worms may invade the bile-ducts and infect the ducts with micro-organisms from the duodenum, and in very rare instances may get into the gall-bladder. In Mertens' [‖] 48 cases of round worms in the bile-ducts five were complicated by calculi. Hanot [**] considered the worms the cause of the calculi, but Mertens thought the calculi dilated the bile-passages and facilitated the entrance of the worms.

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[*] Keith, A.: Lancet, 1903, vol. i, p. 689.

[†] Nauche; Lobstein: Quoted by Trousseau: Clinical Med., vol. iv, p. 230. Translated by New Sydenham Soc.

[‡] Carless, A.: Kings College Hospital Reports, vol. iii, p. 101.

[§] Gautrelet: L'Union Medicale, 1885, No. 138. Quoted by Scheube: Diseases of Warm Countries.

[‖] Mertens: Deutsche med. Wochen., Bd. xxiv, S. 358, 1898.

[**] Hanot: Archiv. général. de Méd., tome clxxvii, p. 74.

Homans[*] records an interesting case in which he removed 97 calculi from the gall-bladder of a woman; twenty months later he again opened the gall-bladder for similar symptoms, and found 7 calculi crystallised on the sutures which lay free in the gall-bladder. In 3 patients operated on by Kehr[†] recurrent colic was found to depend on calculous formation around sutures introduced at the first operation.

Foreign bodies tend to produce stagnation and so favour the production of catarrh if microbes are present; microbes introduced alone may be removed with the bile, but if introduced together with a foreign body, they are enabled, as shown by Mignot's experiments, to induce cholelithiasis.

Catarrhal inflammation of the duodenum and intestinal tract is of great importance in providing micro-organisms to induce similar changes in the gall-bladder.

Excessive eating or drinking, especially alcoholism, tends to induce gastro-intestinal catarrh, and hence cholecystitis and gall-stones are likely to occur in gross feeders, especially when of sedentary habits. Chronic venous engorgement of the portal system, whether from the backward pressure of heart disease, from cirrhosis of the liver or other causes, disposes to catarrh of the gastro-intestinal tract and so to cholelithiasis.

Appendicitis has been thought to give rise to cholecystitis with calculous formation by acting as a primary focus from which virulent coli bacilli may travel to the gall-bladder.

In 18 cases of cholelithiasis operated upon by Ochsner[‡] appendicitis was found in 6. Becker[§] has collected 34 cases in which appendicitis and cholecystitis were associated, and in 720 laparotomies for diseases of the biliary tract Kehr[‖] observed appendicitis in 18, or 2.5 per cent.

On the other hand, the association of appendicitis and cholecystitis has been interpreted in the opposite sense, viz., that infection spreads from the gall-bladder to the appendix. (Dieulafoy.[**])

Relation of Various Factors and Diseases to Cholelithiasis.—*Diet.*—A vegetable diet, by leading to fermentation, is more likely than a mixed or proteid regimen to be followed by gall-stones. It has been thought that a carbohydrate diet disposed to cholecystitis by producing a smaller amount of bile acids, which dissolve cholesterin, than a purely or largely proteid diet.

German soldiers are more often affected with cholelithiasis than English soldiers; this has been correlated with the fact that their daily allowance of meat is 6 ounces as against 12 ounces in the English army. On the other hand, gall-stones are very rare among the natives of India who largely subsist on rice.

The production of gall-stones has been put down to a deficiency in

[*] Homans: Boston Med. and Surg. Journ., July 1, 1897. Annals of Surgery, vol. xxvi, p. 114, 1897 [Plate].

[†] Kehr: Gall-stone Disease, p. 105. American transl., 1901.

[‡] Ochsner: Philadelphia Medical Journal, 1900, p. 652.

[§] Becker: Deutsche Zeitschrift f. Chirurg., Bd. lxvi, S. 246.

[‖] Kehr: Die Therapie der Gallenwege, Bd. iv, S. 456, 1902.

[**] Dieulafoy: La Presse Médicale, June 17, 1903, p. 445.

the solvents of cholesterin, but this is not in accord with Kausch's observation that the solvents of cholesterin are always present in sufficient amounts to dissolve the normal amount of cholesterin. Diet probably disposes to cholelithiasis by setting up dyspepsia and gastro-intestinal catarrh. A saccharine or fatty diet has long been thought to be favourable to the production of gall-stones.

Restriction in the amount of liquid taken by the mouth would tend to diminish the amount of bile and so to impair the freedom with which the ducts are flushed. It is, therefore, reasonable to treat cases of cholelithiasis with free draughts of water, and to believe that an insufficient intake of liquid may act injuriously. On the other hand, in diabetes mellitus, where the polyuria would naturally be expected to diminish the biliary secretion, cholelithiasis is rare. (*Vide* p. 711.) Inasmuch as the amount of calcium in the bile is not affected by that taken by the mouth, it is very improbable that hard water induces cholelithiasis.

Long intervals between meals lead to stagnation of bile in the gall-bladder and so favour infection. Kehr * suggests that the greater frequency of gall-stones among German women as compared with men may depend on their going to bed early and therefore fasting for a number of hours, while late suppers taken by men empty the gall-bladder.

Anxiety and worry have often been regarded as a cause of gall-stones, and possibly act by inducing dyspepsia and constipation and so reducing the resistance of the body as a whole, or possibly of the gall-bladder in particular, and so disposing to infection.

Indigestion is a frequent result of gall-stones; so-called irregular biliary colic not infrequently manifests itself as dyspepsia, and may be due to adhesions between the gall-bladder and stomach. While fully recognising that dyspepsia may be a manifestation of cholelithiasis, there is no doubt that gastro-intestinal catarrh is a very important cause of gall-stones. Abnormal bodies manufactured in the intestinal tract will tend to set up catarrh of the biliary tract, while direct infection *via* the ducts may also be set up. Continued indigestion should be regarded as an important factor in the production of gall-stones.

Constipation may increase intestinal catarrh and so dispose to infection of the gall-bladder; it may also, by leading to fæcal accumulation in the hepatic flexure of the colon, interfere with the flow of bile through the cystic duct and thus produce stagnation in the gall-bladder. Further, intestinal catarrh may be partly due to vigourous purgatives taken in order to get the bowels open.

Kraus † found that 80 per cent. of his patients with gall-stones at Carlsbad had constipation.

Pregnancy.—Gall-stones often develop during or shortly after pregnancy. Naunyn ‡ estimated that 90 per cent. of women with cholelithiasis had borne children. Pregnancy in many women necessitates a very sedentary life, and is frequently accompanied by considerable constipation. It has naturally been thought that the pregnant uterus impedes the descent of the diaphragm and so leads to failure in the expulsion of bile from the gall-bladder. Mosher,[*] however, finds that pregnancy interferes less with the descent of the diaphragm than has been generally thought, and that respiratory movements tend to become equalised so that diaphragmatic respiration persists as late as the eighth month.

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* Kehr: Gall-stone Disease, p. 70. American transl., 1901.

† Kraus: On Gall-stones, p. 20.

‡ Naunyn: On Cholelithiasis, p, 40.

It has been thought that the enlarged uterus may induce compression of the bile-ducts and so favour catarrh of the ducts and cholelithiasis. (Körte, Heddæus.[†])

Repeated pregnancies lead to a relaxed condition of the muscular abdominal walls and so to failure in the expulsion of the contents of the gall-bladder, and may be followed by enteroptosis which may show itself as a floating kidney or unduly movable liver, both of which conditions may interfere with the exit of bile from the gall-bladder.

Glénard's disease or *visceroptosis* may dispose to cholelithiasis in several ways. The liver usually shares in the general prolapse of the abdominal organs, and kinking of or traction on the cystic duct may result and obstruct the exit of bile. While nephroptosis on the right side may also lead to obstruction of the cystic duct, and so favour inflammation of the gall-bladder and the production of gall-stones. From passive engorgement of the intestines catarrhal inflammation may result, and thus tend to lead to the same change in the gall-bladder. Keith [‡] states that gall-stones are almost invariably present in Glénard's disease.

Cardiac disease disposes to cholelithiasis in the first place by rendering life more sedentary and thus leading to stagnation of bile in the gall-bladder, which favours catarrhal inflammation of the gall-bladder. Heart disease, in fact, makes the life of a male much the same as regards its sedentary character as that of women.

In cases of mitral disease with backward pressure gastric and duodenal catarrh are readily set up and thus an ascending inflammation is rendered available. The walls of the gall-bladder may be swollen and chronically engorged, and so more liable to become inflamed should infection be conveyed from the duodenum. The influence of cardiac disease is shown by statistics from the postmortem room.

In 1347 successive autopsies at the Manchester Royal Infirmary gall-stones were found by Brockbank [§] in 101, or in 7.4 per cent. Of these, 504 showed gross cardiac lesions, and in this category calculi were present in 55; or 10.9 per cent. —males, 5.2 per cent.; females, 22.6 per cent.; while in 843 without cardiac disease calculi were met with in 46, or 5.4 per cent.,—males, 3.2, females, 10.2,—so that a gross cardiac lesion seemed to double the incidence of cholelithiasis. This appeared to be almost equally true both for the males and females.

In 200 cases of cardiac disease collected from the postmortem records of St. George's Hospital Dr. F. A. Mills[‖] found that the incidence of cholelithiasis in 119 males was 14, or 11.7 per cent., while in 81 females there were 16, or 19.5 per cent.

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[*] Mosher: Johns Hopkins Bull., Aug., 1901.

[†] Heddæus: Beiträge z. klin. Chirurg., 1894, Bd. xii, S. 439.

[‡] Keith, A.: The Anatomy of Glénard's Disease, London Hospital Gaz., Oct., 1902, p. 60; and Lancet, 1903, vol. i, p. 639.

[§] Brockbank, E. M.: Edin. Med. Jour., vol. iii, p. 51, 1898.

[‖] Mills, F. A.: Unpublished Thesis for M. B. Degree, Cambridge.

From Mills' statistics it appears that the influence of heart disease increases the incidence of calculi relatively more in males than in females, for normally calculi are three times more frequent in females, while in these cases of cardiac disease they are less than twice as common. Mills' statistics also showed that cardiac disease seems to affect the incidence of cholelithiasis by making it occur rather earlier in life than under ordinary conditions.

In Brockbank's statistics mitral stenosis was much the most effective form of heart disease in inducing cholelithiasis; thus in 87 cases gall-stones were present in 19, or 21.8 per cent., this being twice as high as in any other form of cardiac disease. In Mills' 200 cases of cardiac disease the percentage of gall-stones, however, was highest in the aortic cases, 21.6 per cent., and next in mitral disease, 18.75 per cent.

In 20 cases of thoracic aneurysm collected by Mills (18 males, 2 females) there were no calculi; this tends to show that the causes of arterial disease and aneurysm, such as strain, high tension, hard work, syphilis, do not dispose to cholelithiasis. In fact, some of them, almost certainly hard work and exercise, tend to prevent it. The increased incidence of cholelithiasis in cardiac cases is, therefore, due to the effects of the heart lesion and not to causes of cardiac disease, such as strain, high pressure, and so forth.

Pulmonary diseases, such as emphysema, which interfere with the movements of the diaphragm, or conditions such as chronic interstitial pneumonia, advanced emphysema, pneumoconiosis, which lead to failure of the right side of the heart and so to backward pressure, will dispose to gall-stones.

Diabetes.—It might naturally be thought that, owing to the profuse diuresis, the bile would be concentrated and that this would dispose to cholangitis, since the ducts would not be so perfectly flushed. Ascending infection from the duodenum would thus be rendered easier. Most statistics, however, show that biliary calculi are rare in the bodies of patients dying with ordinary diabetes mellitus, and it may, therefore, be assumed that diabetes has no tendency to produce cholelithiasis.

In 220 cases of diabetes collected by Windle * there was only one calculus, or 0.45 per cent. In 142 cases of diabetes (including 122 recorded by Seegen) there was only one where a biliary calculus was mentioned.† This scarcity Brockbank refers to the nitrogenous diet providing plenty of bile acids which keep the cholesterin in solution.

In 27 consecutive cases of diabetes examined at St. George's Hospital calculi were found in 4. These small figures are in antagonism to those quoted above, and are possibly explained by the fact, referred to below, that in two of the four cases the diabetes was really secondary to chronic interstitial pancreatitis set up by gall-stones in the common bile-duct.

But although diabetes does not lead to the production of gall-stones, the converse does not hold good. Thus, if a calculus becomes lodged near the lower end of the common bile-duct, it may lead to infection and chronic interstitial pancreatitis, which may eventually become so extensive as to destroy the islands of Langerhans and set up diabetes mellitus. I have seen at least 2 such cases, which are included among the 4 cases of diabetes at St. George's Hospital which showed cholelithiasis. The occurrence of transient glycosuria during biliary colic is quite another question and is referred to on page 728.

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* Windle: Quoted by Brockbank, On Cholelithiasis, 1896.

† Williamson: Diabetes, p. 119.

To sum up, diabetes does not favour the production of gall-stones, but cholelithiasis may indirectly produce pancreatic diabetes.

In 100 cases of *Bright's disease* Brockbank found 6 cases of gall-stones. Inasmuch as arteriosclerosis and gall-stones both occur about the same period of life, it would be natural to find them often combined.

In 115 cases of cholelithiasis Mosher * found that 50, or 43 per cent., had arteriosclerosis.

Myxœdema.—Many of the conditions favourable to the formation of gall-stones are present in this disease, such as the age (middle life), sex (female), and sedentary habits.†

Both in *portal cirrhosis and in biliary cirrhosis* it is rather surprising that biliary calculi are not commoner. In biliary cirrhosis there is catarrh of the small bile-ducts, and microscopic calculi or plugs of inspissated bile are often seen in the minute bile-ducts and capillaries. In portal cirrhosis a secondary catarrh of the bile-ducts is not infrequent, and is certainly favoured by the condition of the liver.

In 136 cases of cirrhosis examined after death at St. George's Hospital calculi were present in 21, or 15.4 per cent., but in some of these 21 cases there were only small bilirubin-calcium calculi.

Minute bilirubinate of calcium calculi are probably more frequent than is at present known in cases of common or portal cirrhosis; they are small, and may easily escape observation unless carefully sought for.

Malignant Disease.—It was suggested by Musser ‡ that the presence of malignant disease anywhere in the body had a tendency to lead to the formation of calculi in the gall-bladder. It would indeed be natural to expect that gall-stones would be found more frequently in the subjects of malignant disease than in ordinary routine postmortem work; for carcinoma, which is the most frequent form of malignant disease, occurs, like gall-stones, most often in middle and later life, and its victims are often obliged to lead a quiet, sedentary life which tends to biliary stagnation and so favours cholecystitis. It is, therefore, remarkable that the following statistics do not show any increased incidence of gall-stones in patients dying with carcinoma.

In thirteen and one-half years 4236 patients were examined after death at St. George's Hospital. Of these, 242, or 5.7 per cent., had gall-stones. Among the 4236 cases 276 had carcinoma of some part of the body other than the gall-bladder; of these, 16, or 5.7 per cent., had gall-stones (176 males, 5 cases of cholelithiasis, or 2.8 per cent.; 102 females, 11 calculi, or 10.7 per cent.). This incidence of cholelithiasis was highest in primary carcinoma of the liver, uterus, and mamma.

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* Mosher: Johns Hopkins Hosp. Bull., Aug., 1901.

† *Vide* Hertoghe: La Nouvelle Iconographie de la Salpêtrière, 1899.

‡ Musser, J. H.: Boston Med. and Surg. Journ., vol. cxxi.

(J. G. Cooper.*) In 96 cases of malignant disease of various parts of the body collected by Beadles † there was no case of cholelithiasis.

Possibly some statistics of malignant disease may show a high incidence of cholelithiasis, but it must be borne in mind that malignant disease generally is commoner in women than in men, and the influence of sex must not be regarded as the effect of malignant disease. Thus in 44 cases of carcinoma of the mamma gall-stones were present in 16 per cent. (Williams. ‡) Though this percentage would be high for ordinary routine work, it can easily be explained by the influence of sex and age, the subjects of mammary carcinoma being practically always women and usually over thirty-five years of age.

As is well known, gall-stones are present in from 80 to 95 per cent. of cases of primary carcinoma of the gall-bladder, but there can be no doubt that the carcinoma is subsequent to and disposed to by the presence of calculi. (*Vide* p. 627.)

In 13 cases where secondary growths were present in the gall-bladder Siegert § found 2 cases with calculi, and in 13 similar cases, most of which I have examined myself, only one had a calculus. This shows that the local action of a new-growth in the gall-bladder does not favour cholelithiasis.

Uterine fibromyomata are not uncommonly associated with gall-stones.

In 58 cases of gall-stones in women 13, or 22.4 per cent., had fibromyomata. (Mosher. ‖)

Among the insane the percentage of gall-stones in routine postmortem work is much above the average; thus at Colney Hatch Beadles ** finds that 27 per cent. of females and 5 per cent. of males have them, and he quotes Warnock's †† figures of 50 per cent. females and 11 per cent. males dying in Peckham House Asylum to show that this is by no means confined to pauper lunatics.

Cholelithiasis is much commoner in chronic melancholiacs than in acute maniacs; Keay,‡‡ who quotes figures supporting this statement, believes that the stooping position of melancholiacs may play some part in determining the production of gall-stones.

Hereditary Influences.—The idea that cholelithiasis is an hereditary condition depending on an underlying constitutional disposition is a very old one; Morgagni, indeed, insisted on the association of renal and biliary lithiasis, and has been followed by Bouchard, Chauffard,§§ and others who believed that cholelithiasis was a manifestation of the "arthritic" diathesis, which included rheumatism, gout, and "uric acid." Lancereaux‖‖ in 117 cases of much the same condition, which, however, he calls "herpetism," found cholelithiasis in 47. No doubt sedentary habits, overeating, and dyspepsia favour the development of both gout and gall-stones, and, as Senac has shown, the two conditions may occur in the same person; in 166 cases of gall-stones collected by him gout was present in 95. The view that any diathesis plays an important part has not met with so much support since it became clear that local inflammation of the gall-bladder is the immediate cause of gall-stones; Frerichs[*] and Naunyn,[†] in particular, have thrown the weight of their influence against the constitutional factor in cholelithiasis. Quite recently Gilbert and Lereboullet[‡] have laid stress on a family tendency to catarrh of the biliary system (simple family cholæmia) which renders its subjects specially prone to various forms of jaundice, liver disorder, and lithogenic cholecystitis. It is, indeed, probable that this diathesis, though not the sole or most essential factor, is yet of importance in the production of cholelithiasis, while it must not be forgotten that conditions of life and disposing factors, such as obesity, may be transmitted from one generation to another. Some statistics show that gall-stones are hereditary in a large proportion of cases; this was so in 62 per cent. of Kraus' Carlsbad patients.

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* Cooper, J. G.: Unpublished Thesis for M. B., Cambridge, 1903.

† Beadles: Trans. Path. Soc., vol. xlvii, p. 77.

‡ Williams, R.: Brit. Med. Journ., 1893, vol. ii, p. 490.

§ Siegert: Virchow's Archiv, Bd. cxxxiii, S. 353.

‖ Mosher: Johns Hopkins Hosp. Bull., Aug., 1901.

** Beadles: Trans. Path. Soc., vol. xlvii, p. 82.

†† Warnock: Med. Times and Hosp. Gaz., Oct. 13, 1894.

‡‡ Keay: Medical Treatment of Gall-stones, p. 34.

§§ Chauffard: Rev. de Méd., 1897.

‖‖ Lancereaux: Traité des Maladies du foie et du pancreas, p. 686, 1899.

Occupation.—As already pointed out, sedentary occupations dispose to cholecystitis and gall-stones; it therefore occurs more frequently among the rich who are lazy, hard-working literary men, clerks, and devoted men of business, shoemakers, and in the poor in workhouses and asylums than in active persons whether well-to-do or tramps. Davy[§] found that it was rare among soldiers, but possibly this is less true in these days of short service than when he wrote, viz., in the first half of the last century. Among 472 patients at Carlsbad more than 50 per cent. were professors, teachers, officials, or clergymen. (Kraus.[‖])

INCIDENCE.

The incidence of gall-stones in routine postmortem work varies somewhat in different countries between 10 and 6 per cent.

In 10,866 cases obtained by combining the figures of Roth, Schloth, and Schroeder there were 1029 in which gall-stones were present, or 9.4 per cent.[**] This agrees with Kehr's[††] estimate that one-tenth of the adult German population are the subjects of cholelithiasis. In America and England the percentage is lower. In 1655 American cases there were 115, or 6.9 per cent., with gall-stones (Mosher[‡‡]). Voelcker,[§§] at the Middlesex Hospital, found gall-stones in 8.5 per cent. Brockbank,[‖‖] at Manchester, found 101 cases of gall-stones in 1347 autopsies, or 7.4 per cent., while at St. George's Hospital there were 242 in 4236, or 5.7 per cent.[***]

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[*] Frerichs: Diseases of the Liver, vol. ii, p. 511, New Sydenham Soc., 1861.

[†] Naunyn: Cholelithiasis, p. 43, New Sydenham Soc., 1896.

[‡] Gilbert and Lereboullet: Gaz. hebdomen. de Méd. et de Chirurg., Sept. 21, 1902.

[§] Davy, J.: Diseases of the Army, p. 421.

[‖] Kraus: On Gall-stones, p. 19.

[**] Naunyn: Cholelithiasis, p. 144. Transl. New Sydenham Soc.

[††] Kehr: On Gall-stone Disease, p. 99. American transl.

[‡‡] Mosher: Johns Hopkins Hospital Bulletin, Aug., 1901.

[§§] Voelcker, A. F.: Brit. Med. Journ., 1898, vol. ii, p. 1555.

[‖‖] Brockbank: Edinburgh Medical Journ., vol. iii, p. 51, 1898.

[***] For these figures I am indebted to Mr. T. C. English.

The percentage found in bodies examined after death is fairly represented by the statistics of a general hospital. The numbers would, of course, be extremely small in a children's hospital and disproportionately high in a workhouse infirmary.

Race and Geographical Distribution.—Gall-stones are rare in warm and tropical countries and are common in cold and damp cities, probably because these conditions tend to induce catarrh of the biliary tract.

Cholelithiasis is common in Germany, Austria, Sweden, Hungary, Russia, and is said to be infrequent in Holland, Finland, Denmark, and Italy. England probably comes about midway between these two groups. In America the percentage incidence is about the same as in England; thus Mosher found it to be 7 per cent.* The natives of India are remarkably free from gall-stones. Gall-stones are very rare in negroes, probably from their more active life and possibly from the good state of their teeth, in virtue of which they would not be exposed to infection of the alimentary canal from pyorrhœa alveolaris.

In America cholelithiasis is less common in coloured than in white patients; in 106 cases of gall-stones operated upon in Louisville only one was coloured.† In routine postmortem examination at the Johns Hopkins Hospital, Baltimore, however, the percentage incidence of gall-stones among blacks was 5.5 as against 7.9 among whites.

In England a large number of cases come from the east coast, especially Lincolnshire. Ralfe ‡ says that the bleak country between Stafford and Wolverhampton furnishes a high percentage of cases, and that the damp valleys in Wales are responsible for many cases. Keay § considers that it is commoner in Lancashire than in London.

Age.—The incidence of gall-stones increases as age advances. The majority of patients with cholelithiasis are over forty years of age, and it is rare before thirty.

Harley ‖ gives the following estimate: 75 per cent. of cases occur in persons over forty; 20 per cent. between thirty and forty; 4 per cent. between twenty and thirty; 1 per cent. under twenty.

In Brockbank's ** 101 cases of cholelithiasis 79 were over and 22 under forty years of age. In 242 cases in which gall-stones were found at St. George's Hospital 199, or 82 per cent., were forty or over. The largest number were between the ages of fifty and sixty; of the 242 cases, 89, or 37 per cent., were in this decade.

The frequency of biliary calculi in the gall-bladder of old people may possibly be due to senile atrophy of the smooth muscular tissue in the walls of the gall-bladder and bile-ducts (Charcot and Pitres††), which, by leading to some degree of stagnation, favours infection and at the same time interferes with the expulsion of any calculi that are formed. Thus, while calculi are very frequent in the bodies of old persons, especially in asylums and workhouses, symptoms of biliary colic are comparatively rare.

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* Mosher: Johns Hopkins Hosp. Bull., Aug., 1901.

† International Text-book of Surgery, Gould and Warren, vol. ii, p. 741.

‡ Ralfe: Clin. Journ., Sept. 4, 1895.

§ Keay: Medical Treatment of Gall-stones, p. 27.

‖ Harley, G.: Diseases of the Liver, 1883, p. 577.

** Brockbank, E. M.: Edinburgh Medical Journal, 1898, vol. iii, p. 51.

†† Charcot and Pitres: Quoted by Waring: Diseases of Liver, p. 218.

Cholelithiasis in Early Life.—Calculi are rare under twenty years of age. When cholelithiasis does occur in early life, the cases may be divided into two classes:

(i) Those in which the processes begins in intra-uterine life. A striking example of this category is Wendel's[*] case of a child eleven days old in whose gall-bladder there were 90 small cholesterin calculi. Thomson[†] has collected 7 cases of jaundice in infants either still-born or dying within the first month, in which gall-stones were present in the ducts. He makes the very probable suggestion that gall-stone formation in infants and congenital obliteration of the ducts are dependent on the same inflammatory process. Still[‡] has collected 10 cases, including Thomson's 7, in which small calculi were present in infants dying within a month of their birth.

(ii) Calculi found in children. It is hard to draw a hard-and-fast line between these two categories, and very possibly in cases where the clinical manifestations are first noticed months or years after birth the process began in intra-uterine life or depended, as Albu[§] has suggested, on some change in the ducts allied to congenital obliteration of the ducts. Cholecystitis from typhoidal or colon infection may occur in early life; it is, indeed, rather surprising, in the face of the frequency of various forms of gastro-intestinal infection in early life, that cholecystitis is so rare. It has been suggested that the application of a tight binder to a child's abdomen should, by inducing biliary stasis, dispose to the formation of calculi. (Wendel.) Small bilirubin-calcium calculi may be found in cases of biliary cirrhosis, and are then due to inflammation spreading from the smallest bile-ducts—a descending cholangitis.

A number of cases between three and fifteen years have been collected by Gourdin Serveniere[‖] and Mercat.[**] Trousseau[††] had previously described one in a girl aged nine years.

Sex.—Gall-stones are more frequent in the female than in the male sex; the ratio has been variously estimated at from five to one to four to three. Schroeder[‡‡] found gall-stones five times in females to once in males; Brockbank,[§§] four times in females to once in males; Harley[‖‖] and Kraus,[***] twice in females to once in males; Mosher,[†††] three times in females to twice in males. In 242 cases in which gall-stones were found after death at St. George's Hospital the number of women (136) was in excess of the males (106) in the ratio of 4 to 3.

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[*] Wendel: Medical Record (N. Y.), July 9, 1898, p. 41.

[†] Thomson, J.: Edinburgh Hosp. Reports, vol. v.

[‡] Still, G. F.: Trans. Path. Soc., vol. l, p. 154.

[§] Albu: Deutsche med. Wochen., March 31, 1898, S. 201.

[‖] Serveniere: Thèse Paris, 1889.

[**] Mercat: Thèse Paris, 1884.

[††] Trousseau: Clinical Medicine, vol. iv, p. 224. Transl. New Sydenham Soc.

[‡‡] Schroeder: Quoted by Naunyn, Cholelithiasis, p. 40.

[§§] Brockbank: Loc. cit.

[‖‖] Harley: Diseases of Liver, p. 575, 1883.

[***] Kraus: On Gall-stones, English translation, p. 2, 1896.

[†††] Mosher: Johns Hopkins Hospital Bulletin, Aug., 1901.

The factors determining the greater incidence of gall-stones in women are:

(i) A lax condition of the abdominal walls, which favours visceroptosis and may even produce hepatoptosis. As a result, stagnation of bile in the gall-bladder, a condition disposing to infection, is brought about. (ii) Abdominal tumors, such as uterine myomata, ovarian cysts, and the pregnant uterus produce relaxation of the abdominal wall and interfere with diaphragmatic respiration. (iii) Tight lacing may act in several ways: by displacing the liver it may kink the common or cystic ducts and mechanically obstruct the outflow of bile from the gall-bladder. It also tends to diminish diaphragmatic breathing and to increase costal respiration. The movements of the diaphragm are of importance in emptying the gall-bladder, and hence if they are diminished, stagnation of bile follows. (iv) The more sedentary life led by most women. (v) Constipation is commoner in women and is favourable to infection of the bile-ducts and gall-bladder. (vi) Pregnancy. (*Vide* p. 709.) (vii) The frequency of inflammatory pelvic conditions in women has been urged by Mosher * as a cause of the greater incidence of gall-stones among women. The resulting peritoneal adhesions may indirectly exert some mechanical difficulties to the free exit of bile from the gall-bladder, while at the outset infection may be carried to the gall-bladder.

CLASSIFICATION OF GALL-STONES.

The following classification of gall-stones, according to their chemical composition, is given by Naunyn:

I. *Pure cholesterin calculi* are comparatively uncommon. They are white, yellow, or more rarely brown or greenish, and have a translucent appearance. The surface is nodular, crystalline, or smooth, but hardly ever facetted. On section they are crystalline, but not stratified.

II. *Laminated cholesterin calculi* contain 90 per cent. of cholesterin, with calcium carbonate and traces of bilirubin and biliverdin in combination with calcium. Externally they resemble pure cholesterin calculi, but are often facetted. On section, there are alternating laminæ—white and brown, yellow or green. The coloured layers contain bilirubin-calcium when brown, and biliverdin-calcium and calcium carbonate when green.

III. *The Common Gall-stones* (*Mixed Cholesterin Calculi*).—They vary in size and colour. They are usually facetted, are seldom larger than a cherry, and may be very small and numerous. They are usually yellow, but may be brown or white. When fresh, they are greasy and soft, but when dried, they become hard externally. There may be a central cavity inside.

IV. *Mixed bilirubin and cholesterin calculi* contain as much as 25 per cent. of cholesterin, the remainder being bilirubin-calcium. They occur in the gall-bladder or large bile-ducts, and consist of a nucleus of cholesterin covered by thick layers of dark-brown material which readily chips off.

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* Mosher: Johns Hopkins Hosp. Bull., Aug., 1901.

V. *Pure Bilirubin-calcium Calculi.*—They vary from the size of a pea to a grain of sand. There are two types: one is solid, brown in colour, rough on the surface, and with a tendency to become welded together. The second type is harder, smooth, black, has a metallic lustre, and internally a spongy structure.

VI. *Rarer Forms.*—(*a*) *Amorphous and incompletely crystalline cholesterin gravel:* these small calculi may look like pearls; the nucleus is of different composition—often of bilirubin cholesterin. (*b*) *Calcium carbonate calculi* are very infrequently seen. (*c*) *Calculi containing foreign bodies*, such as fragments of worms, ligatures (*vide* p. 709). (*d*) *Conglomerate calculi*, which are composed of two or more small calculi united under a common sheath. (*e*) *Casts of bile-ducts* are very rare in man; bilirubin-calcium casts are found in cattle.

MODE OF FORMATION OF CALCULI IN THE GALL-BLADDER.

The cholesterin from which the calculi are, in the first instance, largely formed, is not derived from the bile itself, but from the disintegration of the cells lining the gall-bladder, and is the outcome of perverted metabolism induced by catarrh. Inside the cells of an inflamed gall-bladder myelin bodies—the precursors of cholesterin—can be seen. Cholesterin is formed by other mucous surfaces, but calculus formation does not result, since there is an absence of the necessary cementing substance. According to Naunyn, the cementing substance is present in the gall-bladder in the form of bilirubin-calcium. Masses of cholesterin mixed with bilirubin-calcium form the earliest stage of a calculus. The further development, according to Naunyn, may proceed in different ways: The mass may become surrounded with a firm crust of bilirubin-calcium, while the cholesterin and bilirubin-calcium crystallise out on the inner surface of the outer crust, thus leaving a central cavity. Or the firm outer layer may be produced by drying, starting in the outer layer of the mass of bilirubin-calcium and cholesterin, after which crystallisation takes place inside the shell with the production of a central cavity as before. So far as the formation of an immature calculus has been traced, the further changes leading to the growth and formation of a stratified and more solid calculus are as follows:

The growth of a calculus is chiefly the result of deposition, on its surface, of concentric layers of cholesterin and of bilirubin-calcium or biliverdin-calcium. The cholesterin forms white laminæ, and is deposited, not as crystals, but as a pultaceous mass of myelin bodies supplied by the cells of the gall-bladder. In the formation of pure cholesterin calculi the gall-bladder contents must be free from any bile, as in cases of obstruction of the cystic duct. Bilirubin-calcium forms brown strata, while biliverdin produces green strata; their deposition occurs when the gall-bladder contains bile.

An important change by which the calculus becomes affected is the infiltration of its substance from without by cholesterin, exactly in the same way as a calculus in the urinary bladder is invaded by phosphates and other salts. The secondary infiltration of a gall-stone with cholesterin may be derived from the epithelial walls of the gall-bladder if in contact with it, or from the cholesterin in the bile. The cholesterin tracks along small fissures and canals in the calculus, and penetrates into its interior; it then crystallises, and these crystals increase in size. This process begins at the centre, and spreads outwards towards the periphery. While this permeation with cholesterin is proceeding the bilirubin-calcium is dissolved out, and the percentage of cholesterin increases; in this way a pure cholesterin calculus may be produced.

Time Required for the Formation of Calculi.—From his experimental researches Mignot * believes that it takes five or six months to form a stratified, well-formed biliary calculus. For this it is necessary that there should be comparative stagnation of bile, otherwise the soft, immature calculus would be expelled with the bile from the gall-bladder. Calculi found in the gall-bladder may be all of the same age and due to one and the same attack of cholecystitis, which is a transitory event. If recurrent attacks occur,—and this readily may take place in a damaged gall-bladder,—fresh calculi may be formed.

The formation of calculi in the ducts is described under the immediate causes of cholelithiasis.

Size and Number.—There may be one or almost any number of calculi in the gall-bladder. A single calculus may be very large and cause great distension of the gall-bladder.

Meckel recorded a calculus 6½ inches long and 6 inches thick. A large single calculus is usually a laminated or a pure cholesterin stone.

In Fiedler's † case a calculus weighed 46 grammes (1½ ounces) and consisted of three pieces which fitted together to form a cast of the elongated gall-bladder and was at least 12 inches long. Richter ‡ in 1793 recorded an enormous calculus weighing 3 ounces 5 drachms, which is the largest ever described. (Mayo Robson.§)

Occasionally very large numbers of small calculi are found in the gall-bladder.

Naunyn ‖ counted 5000 in a gall-bladder, but this is surpassed by 7802 in Otto's ** case.

The small calculi found in such large number are curiously alike in appearance, and are generally of the mixed cholesterin form.

Shape.—There is a great deal of variation in the shape of biliary calculi, which largely depends on their surroundings. Apart from external influences, calculi probably tend to be round.

The large single stone filling up the gall-bladder is usually somewhat elongated and pear-shaped, and may be conglomerate from the union and welding together of previously separate calculi. A single loose calculus, when composed of pure cholesterin, is often bossed like a mulberry calculus in the kidney. Multiple gall-stones in the gall-bladder are sometimes round, but are more often irregularly square, with facets separated by rounded edges. When impacted in the commencement of the cystic duct, a calculus may be somewhat elongated.

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* Mignot, R.: Thèse Paris, 1897, and Archiv. général. de Méd., Aug., 1898.

† Fiedler: Jahresbericht d. Gesellschaft f. Nat. u. Heilk., Dresden, 1879.

‡ *Vide* Hutchinson's Archives of Surgery, vol. iii, p. 6, 1892.

§ Diseases of Gall-bladder, p. 215, ed. iii.

‖ Naunyn: On Cholelithiasis, p. 6. Translat. New Sydenham Soc.

** Otto: Quoted by G. Harley, Diseases of the Liver, p. 583, 1883.

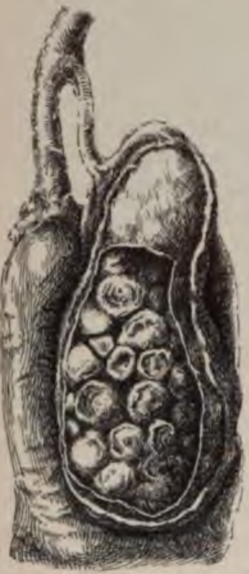
FIG. 93.—DRAWING OF A GALL-BLADDER IN ST. GEORGE'S HOSPITAL MUSEUM, DISTENDED WITH A NUMBER OF FACETTED GALL-STONES. (Drawn by Dr. E. A. Wilson.)

Crumbling calculi in the common bile-duct become elongated and moulded to the duct. The small bilirubin-calcium calculi formed in the intra-hepatic ducts are elongated and represent the lumen of the duct in which they were formed. Occasionally branching calculi resembling coral are found in the larger intra-hepatic ducts.

Situation.—Calculi in the gall-bladder are usually loose in the bile, or, when the cystic duct has been permanently blocked for some time, in the mucus. In some cases the gall-bladder is firmly contracted on the calculus. In some instances the gall-bladder may contain a large number of calculi closely packed and facetted on each other, there being no bile or mucus in the gall-bladder.

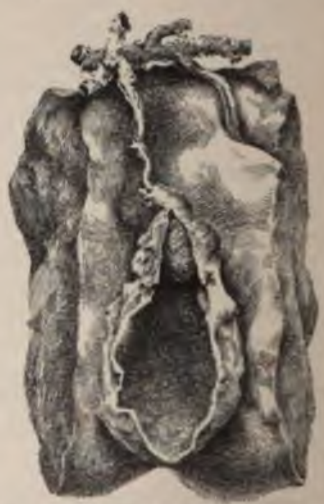
FIG. 94.—A CALCULUS IMPACTED IN THE NECK OF THE GALL-BLADDER. (Drawn by Dr. E. A. Wilson.)

In cases where the gall-bladder is thus distended with calculi a crackling sensation may sometimes be felt on palpation.

A large gall-stone may be adherent to the mucous membrane of the gall-bladder. In an hour-glass gall-bladder calculi contained in the distal compartment may be closely united to the mucous membrane. It is comparatively common to find a calculus impacted in the neck of the gall-bladder and thus obstructing the orifice of the cystic duct.

Calculi, or masses of cholesterin which hardly deserve the name of calculi, are sometimes found embedded in the wall of the gall-bladder. This has a direct relation to the manufacture of cholesterin by the mucous membrane of the gall-bladder and of its mucous glands.

In a case of parietal calculi recorded by Peraire * there were a series of gall-stones embedded in the wall of the gall-bladder, and 27 calculi the size of peas in the lumen of the cystic duct, but none in the cavity of the gall-bladder.

A gall-stone may set up ulceration and weakening of the gall-bladder, and may thus form for itself a kind of diverticulum in which it becomes encysted. This is a rare event, and is more often seen near the fundus or at the neck of the gall-bladder. Under ordinary conditions the calculi are naturally usually found lying in the fundus of the gall-bladder.

The occurrence of calçuli in the cystic and common bile-duct is referred to elsewhere. (*Vide* pp. 737 and 739.) In rare instances a calculus derived from the gall-bladder passes backwards from the cystic duct into the common hepatic duct.

An olive-shaped calculus the size of a small pigeon's-egg was removed from the common hepatic duct of a woman aged sixty-seven years by Le Filliatre.†

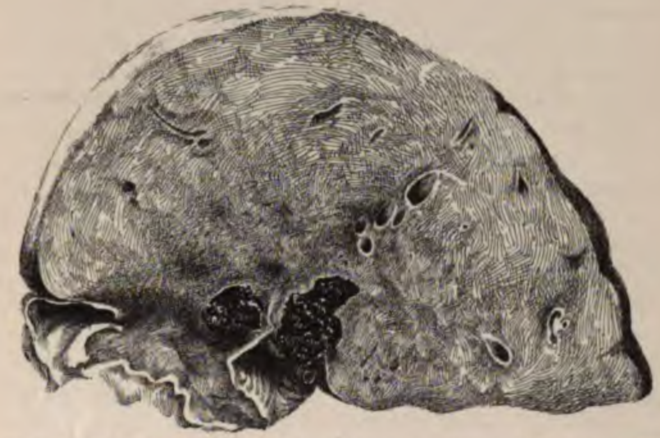

FIG. 95.—LARGE INTRA-HEPATIC CALCULI DISTENDING THE RIGHT AND LEFT HEPATIC DUCTS. (Drawn by Dr. E. A. Wilson.)

Intra-hepatic Calculi.—Large intra-hepatic calculi occupying the hepatic ducts and distending them are very rare. I met with one such case in a man who died with diabetes from secondary chronic pancreatitis.‡ (*Vide* Fig. 95.)

Murchison § refers to a plate of Cruveilhier's (livraison xii, Plate V), showing large branching intra-hepatic calculi like coral. There is a good specimen of multiple intra-hepatic calculi in the Westminster Hospital Museum (No. 581). These calculi almost necessarily set up jaundice and a good deal of pericholangitis, which may be suppurative. The calculi are chiefly composed of bilirubin-calcium. Small black bilirubin-calcium calculi are not uncommon.

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* Peraire: Bull. Soc. Anat. Paris, 1902, p. 707.

† Le Filliatre: Bull. Soc. Anat. Paris, 1900, p. 626.

‡ Rolleston: Trans. Path. Soc., vol. xlix, p. 133.

§ Murchison: Diseases of Liver, 2d ed., p. 545.

Occasionally masses of calculous material are found embedded in the substance of the liver in dilated, ampulla-like terminations of bile-ducts which have lost their continuity with the bile-ducts.

Small *facets* on the surface of gall-stones show that there either are or have been more than one calculus in the gall-bladder or ducts. Two or more facets on one calculus are in favour of the number of stones being more than two. Facetting generally indicates that the calculi have been closely packed.

Facetting is commoner on medium-sized stones, but may be seen on comparatively large calculi. In small bilirubin-calcium calculi which are freely movable on each other there are no facets as a rule.

Spontaneous Fracture of Gall-stones in the Gall-bladder.—Cases in which a gall-stone has been found to have broken up within the gall-bladder have been reported by Pearce Gould,* Hadden,† Calvert,‡ and myself.§ Traumatism during life or in the course of the postmortem examination appears to have been excluded, and, though conceivable, it does not seem very likely that vigourous contraction of the gall-bladder would fracture even a friable calculus. It is more probable that the fracture is brought about in much the same way as spontaneous fracture of vesical calculi in the urinary bladder, as explained by W. M. Ord,‖ and Plowright.** It is known that under ordinary conditions cholesterin works its way in, while bilirubin-calcium passes out, of biliary calculi. Chauffard †† and others have shown that micro-organisms of the colon group may also pass in. By forming a deposit between the layers of the calculus this microbic invasion would tend to loosen and split off the more superficial layers of the calculus.

It was suggested by Calvert that fracture might depend on drying of a calculus. It is conceivable that in some instances the union and subsequent disruption of a number of calculi might imitate spontaneous fracture. Care must also be taken not to regard as examples of spontaneous fracture marked facetting of the surfaces of adjacent calculi.

CLINICAL PICTURE.

Gall-stones are frequently present in the gall-bladder without giving rise to any symptoms. Kehr ‡‡ states that symptoms occur in only 5 per cent. of persons whose gall-bladders contain calculi. This latency is especially common in old people, in whom the muscular tissue of the gall-bladder and ducts is atrophied, and it has been thought that for this reason the passage of a calculus out of the gall-bladder into the ducts is less likely to occur.

The symptoms produced by gall-stones are extremely numerous and

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* Pearce Gould: Trans. Clinic. Soc., vol. xxi, p. 193.

† Hadden, W. B.: Trans. Path. Soc., vol. xli, p. 160.

‡ Calvert, J.: Trans. Path. Soc., vol. xlix, p. 139.

§ Rolleston, H. D.: Trans. Path. Soc., vol. xlix, p. 135.

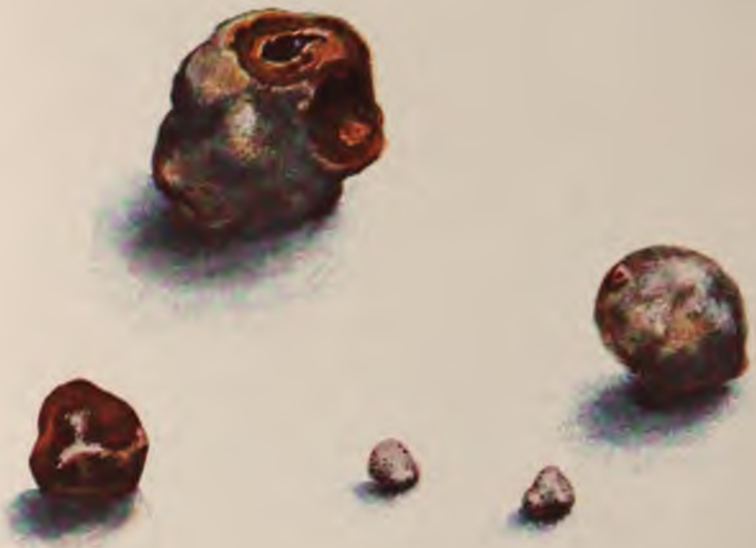
‖ Ord, W. M.: Trans. Path. Soc., vol. xxviii, p. 170; vol. xxxii, p. 304.

** Plowright: Trans. Path. Soc., vol. xlvii, p. 132.

†† Chauffard: Rev. de Méd., Feb., 1897.

‡‡ Kehr, H.: Diagnosis of Gall-stone Disease, p. 25, American translat.

PLATE 6.



GALL-STONES FROM A CASE IN WHICH FRACTURE WAS SPONTANEOUS.

The largest calculus shows surface where spontaneous fracture has occurred. The calculus below and to the left fitted into it. The other calculi were in the same gall-bladder. From a case of primary carcinoma of the gall-bladder in which spontaneous fracture of the calculi had occurred. Painted by Dr. E. A. Wilson.

variable. It will be most satisfactory to divide their description into that of—(i) Biliary colic; (ii) the purely mechanical or aseptic effects of gall-stones; and (iii) the inflammatory and infective changes set up by cholelithiasis; special descriptions will be given of intestinal obstruction and of fistulæ produced by gall-stones, under the headings of (ii) and (iii) respectively.

BILIARY COLIC.

Typical biliary colic is generally regarded as the result of spasm set up by the passage of a calculus down the cystic and common bile-ducts. Attacks of pain of less severity may possibly be due to spasm set up by a stone in the gall-bladder which has not actually entered the cystic duct. Inspissated bile and precipitated masses of cholesterin and bile-pigments in the ducts may also induce modified attacks of biliary colic. Inflammation and spasm extending to the ducts from cholecystitis must also be reckoned with as a cause of biliary colic. In other words, biliary colic may, like the pain of appendicitis, be independent of calculi. Cholecystitis with closure of the cystic duct from any cause will give rise to painful contractions of the gall-bladder; in many cases the factor responsible for closure of the cystic duct is a calculus.

In recent times some writers, such as Riedel* and Kehr, have minimised the purely mechanical rôle of calculi in the production of biliary colic, and have insisted on the importance of cholecystitis and on the extension of inflammation to the ducts as the cause of pain and jaundice. But while inflammatory obstruction of the cystic duct is quite enough to set up painful contractions of an inflamed gall-bladder, there is no reason to doubt that the mechanical irritation of a calculus in the ducts sets up spasm and colic in the same way that a calculus in the ureter causes renal colic. In other words, biliary colic may be due to inflammatory or to mechanical obstruction, or to both combined.

Cause of the Passage of Calculi out of the Gall-bladder.—Gall-stones are very commonly latent in the gall-bladder; it has, indeed, as mentioned above, been estimated that only 5 per cent. of persons with gall-stones in the gall-bladder suffer from them.† It is, therefore, clear that some conditions other than those of ordinary life must be responsible for the passage of calculi into the cystic duct, and that something more is required than the ordinary muscular contractions of the gall-bladder which suffice to drive out the bile. It has been thought that unusually vigourous contractions of the gall-bladder, such as might be induced by violent emotion, may determine the passage of gall-stones into the cystic duct. The onset of colic at the menstrual periods has been referred to spasmodic contraction of the gall-bladder set up by nervous perturbation. Occasionally jolting, such as riding in a cart without springs, a railway journey, riding a bicycle, etc., has been thought to determine the passage of calculi into the cystic duct. Keay ‡ believes that pain following jolting is due to stretching of adhesions rather than to the passage of gall-stones, and that a stooping posture favours the migration of a calculus out of the gall-bladder. Von Noorden * has pointed out that biliary colic may occur in patients immediately after treatment for obesity, and suggests that the removal of fat allows the pressure of corsets to interfere with the flow of bile out of the gall-bladder.

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* Riedel: Berlin. med. Wochen., Bd. xxxviii, S. i, 1901.

† Kehr, H.: Diagnosis of Gall-stone Disease, p. 25. American translation.

‡ Keay: Medical Treatment of Gall-stones, p. 37.

Clinical palpation of the gall-bladder is certainly sometimes followed by colic, but it can be very rarely that the stone is directly forced into the cystic duct. Traumatism, such as a fall or blow, may, by reducing the resistance of the gall-bladder, allow micro-organisms to set up cholecystitis and so lead to the expulsion of a calculus into the ducts.

While not denying the possibility that the contractions of the gall-bladder may drive calculi into the cystic and common bile-duct, Kehr † believes that the important factor in determining the migration of calculi from the gall-bladder into the ducts is inflammation of the gall-bladder. The mechanism is as follows: Cholecystitis gives rise to an inflammatory exudation which distends the gall-bladder and drives the calculus into the cystic duct. Enlargement of the gall-bladder, tenderness, and fever during biliary colic are in favour of the view that cholecystitis plays an important part in its production. When the calculus is impacted in the duct, it will mechanically set up painful spasm of the ducts and gall-bladder. Acute cholecystitis may be set up by microbic infection derived either from the intestine or from the general circulation. Diarrhœa, typhoid fever, influenza, may thus be antecedent conditions to an attack of biliary colic.

Onset.—The extremely violent pain of biliary colic may come on quite suddenly, or may be preceded by symptoms, such as shivering, nausea, and vomiting, compatible with the view that cholecystitis is in progress. Formerly the entrance of a gall-stone into the cystic duct was thought to be the outcome of contractions of the gall-bladder set up reflexly by the passage of food into the duodenum, and three to four hours after food was thought to be a specially probable time for the onset of biliary colic. Biliary colic more commonly commences at night.

The onset of the menstrual period has been thought, by inducing nervous disturbance and general engorgement of the abdominal viscera, to determine an attack of biliary colic.‡ During pregnancy and lactation biliary colic is either less frequent or absent, but after weaning the child severe attacks may occur. As has already been pointed out, pregnancy favours the production of gall-stones. (*Vide* p. 709.) After delivery conditions leading to infection of the gall-bladder are not uncommon, and thus the onset of colic may be determined.

Signs and Symptoms.—*The pain* in biliary colic is due to two factors —in the first instance, there is probably nearly always acute inflammation of the gall-bladder, which precedes and may be the determining factor in the expulsion of calculi into the cystic duct. The pain of acute cholecystitis is felt in the right hypochondrium and epigastrium. When the calculi pass into the cystic duct, severe muscular spasm is set up, which manifests itself by pain in the right loin and back. Keay,* from personal experience and from observation of patients, believes that pain depending on the presence of a calculus in the cystic duct begins to the right of the region between the eighth and eleventh dorsal vertebræ. In this view Keay differs from most authorities, such as Naunyn, who state that the pain begins in the epigastrium or right hypochondrium. This pain is extremely severe, as if the back was being broken. It passes to the right hypochondrium and radiates from this spot in all directions—to the left hypochondrium, the umbilical and hypogastric regions, to the thighs, and even to the arms and neck. The pain is usually stated to radiate to the right shoulder, but this is less frequent in biliary colic than in hepatic abscess.

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* Von Noorden, C.: Diseases of the Metabolism and Nutrition, Part I, Obesity, p. 31, 1903. E. B. Treat and Co., New York.

† Kehr: Loc. cit., p. 26.

‡ Cornillon: Le progrés Méd., April 24, 1897.

The pain, which is usually paroxysmal, is probably one of the most agonising forms humanity is subject to; women speak of it as being much worse than the pains of labour. The intensity of the pain may give rise to hysterical or epileptiform attacks, and in very rare cases the patients have died apparently simply from the shock of the pain. (Allbutt,† Mayo Robson.‡)

The pain is so excruciating that the patient throws himself into various positions to obtain relief, but without any success. He may roll in agony on the floor and scream, cry, or groan in a very distressing manner. The intense pain gradually diminishes, and the patient experiences a constant dull aching which is interrupted by paroxysms of intense pain. It is supposed that alleviation of the pain may coincide with the passage of the calculus out of the small cystic duct into the larger common bile-duct.

The first attack is nearly always much more severe than subsequent seizures, and it is believed that a small calculus in a first attack may give rise to far more pain than larger gall-stones on subsequent occasions. There is thus no absolute relationship between the size of the calculi and the severity of the pain. The ducts become dilated by the passage of successive calculi, and eventually a large one may pass almost unnoticed.

Pain may suddenly disappear as if by magic, and may be due to the escape of the calculus into the duodenum. Keay believes that at the moment when the stones pass into the duodenum there is a peculiar gliding sensation to the right of the tenth and twelfth dorsal vertebræ.

The violent pain usually lasts for some hours—three to twelve—if unrelieved by morphia. In rare instances it may only last for a few minutes.

The pain is sometimes described as lasting for days, but this is probably due to a succession of attacks supervening rapidly, with pain of a less severe character, due to the inflamed or distended and inflamed gall-bladder, in the intervals between the more severe paroxysms.

It has been estimated that the temperature is raised in 60 per cent.

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* Keay: Brit. Med. Journ., 1900, vol. i, p. 901. Medical Treatment of Gall-stones, p. 75.

† Allbutt: In his System of Medicine, vol. iii, 471.

‡ Mayo Robson: Allbutt's System of Med., vol. iv, p. 238.

of the cases. The fever is well explained on the ground that there is concomitant cholecystitis or cholangitis, and in some instances there is palpable and tender enlargement of the gall-bladder and may be splenic enlargement and albuminuria to lend support to the theory of infection. The mechanism is much the same as in intermittent hepatic fever (*vide* p. 751) from which, however, it differs in being acute.

The fever was formerly thought to be reflex in origin, and due to the violent nervous stimuli accompanying the colic. Such a view is to some extent supported by cases in which at operation there is no manifest inflammation of the gall-bladder or ducts. Nevertheless even in such cases it is not unreasonable to believe that there is some degree of infection sufficient to induce fever, though not to produce naked-eye changes.

Boix * has suggested that during an attack of biliary colic the detoxicating function of the liver is suspended and that poisonous bodies absorbed from the intestinal tract, and usually stopped or rendered harmless by the liver, thus pass into the general circulation and give rise to pyrexia.

Reflex vomiting accompanies the intense pain, and is often followed by some relief. The contents of the stomach are first brought up, and subsequently those of the duodenum; in very rare instances a calculus has been vomited. There is usually bile in the vomit, which suggests that at this period the common duct is not completely occluded. Dyspepsia and flatulence may accompany or follow the attack. There is naturally distaste for food, though thirst may be urgent. Constipation is usually present. Where jaundice is already marked, the fæces may be devoid of bile, but this is far from invariable.

The abdomen is usually somewhat retracted from vigourous contraction of the abdominal muscles. Occasionally there is considerable tympanitic distension, but, according to Naunyn, this is seen only in persons habitually subject to flatulence. Transient dilatation of the stomach has been described. There is tenderness over the situation of the gall-bladder and sometimes over the liver.

Enlargement of the liver is present in some instances, but very frequently its presence or absence is difficult to determine, as the hypochondrium is extremely tender and the patient, being in great pain, is naturally far from tolerant of examination, while the recti are rigid and interfere with accurate palpation. The swelling of the liver may be explained as partly due to inflammation of the bile-ducts and partly to retention in the liver of bile from the obstruction. Tenderness of the liver is often present without any manifest enlargement. The gall-bladder is probably frequently enlarged from accompanying cholecystitis, but its examination is far from easy, as there are usually considerable tenderness over the gall-bladder and rigidity of the abdominal muscles.

Naunyn estimates that the gall-bladder is only palpable in one-third of the cases of biliary colic.

The spleen is only enlarged in cases where there are severe infective processes at work.

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* Boix, E.: Archiv. général. de Méd., 1901, t. clxxxviii, p. 466.

During a paroxysm the skin is hot and moist or bathed in perspiration, and there may be rigors or shivering.

From the intense pain there is considerable prostration, which remains for a time after the paroxysm has passed off.

Nervous symptoms occasionally accompany biliary colic and are due to the intense visceral pain. Various hysterical manifestations * or epileptiform convulsions may occur. Sudden death during a paroxysm of pain, due to cardiac inhibition brought on reflexly through the vagus, has been recorded in rare instances.

Naunyn † refers to nine cases in which death took place during severe attacks of biliary colic; Clifford Allbutt,‡ Mayo Robson,§ and Calvert ‖ have also referred to similar cases.

In exceptional instances temporary hemiplegia, paraplegia, or even tetany have been observed in biliary colic. Sleepiness and drowsiness may naturally follow attacks of biliary colic and be due to nervous exhaustion, to the presence of bile in the circulation, or in some degree to the effects of morphia given for the relief of the paroxysmal pain.

Extreme drowsiness was a striking feature in a woman aged thirty who had suffered from gall-stone colic for six years. (Levi.**)

Kehr †† states that patients subject to gall-stone colic frequently suffer from attacks of migraine, which, however, disappear when the calculi are removed by operation. During biliary colic hiccough may occur.

There may be a dry cough due to reflex irritation. Reflex constriction of the vessels in the lungs with rise of blood-pressure in the pulmonary artery, as shown by accentuation of the second sound over the pulmonary artery, has been described and is supported by the experimental observation that irritation of the bile-duct induces a reflex constriction of the pulmonary vessels. (Francois-Franck and Arloing.) Signs of congestion of the base of the right lung, and, in very exceptional instances, hæmoptysis (Cassouti ‡‡), have been observed. Dilatation of the right side of the heart has been described and has been referred by Potain to the rise of pulmonary blood-pressure. It may also be due in some measure to the action of poisons absorbed from the bile-ducts or in some cases from the effect of bile salts in the blood. Temporary dilatation of the left ventricle with a systolic apical murmur may also be met with.

There may be palpitation, disturbed cardiac rhythm, with rapid action, irregularity, or even slowing of the heart. The pulse during a paroxysm becomes small, feeble, and is generally of about the normal rate; in some cases it is even slower than normal. Kraus* observed a pulse of 42 in one case.

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* Jeanselme et Rabé: Soc. Méd. des Hôp., July 15, 1898.

† Naunyn: Cholelithiasis, p. 89. Transl. New Sydenham Soc.

‡ Allbutt, in System of Medicine, vol. iii, p. 471.

§ Mayo Robson: Gall-stones, 1892.

‖ Calvert, J. T.: Indian Med. Gaz., vol. xxxviii, p. 413.

** Levi: Archiv. général. de Méd., t. clxxvii, p. 63, 1896.

†† Kehr: Diagnosis of Gall-stone Disease, American transl., p. 56.

‡‡ Cassouti: Bulletin Med., No. 70, 1897.

Examination of the blood shows that there may be no leucocytosis in severe biliary colic, while in other cases it may be present in a moderate degree. The factors determining the presence or absence of leucocytosis are probably the extent and character of the cholecystitis; if there is catarrhal inflammation, there is no increase in the number of leucocytes, while in suppurative cholecystitis there may be considerable leucocytosis. (Ewing.†) Albuminuria is not infrequent, and transient glycosuria is occasionally observed during a paroxysm. There is some difference of opinion as to the frequency with which glycosuria occurs. It has been referred to the widespread nervous disturbance, but it is conceivable that it is toxic.

True diabetes may be the result of chronic pancreatitis set up by a calculus in the lower part of the common bile-duct, but these cases are not often the subject of typical severe attacks of biliary colic. Conversely in two well-marked cases of diabetes mellitus Gilbert and E. Weil ‡ observed that during intercurrent attacks of hepatic colic the glycosuria diminished.

Bile-pigment occurs in the urine before there is any manifest jaundice; the presence of bile in the urine may be quite transient and may be succeeded by an excessive amount of urobilin.

Indican does not occur in uncomplicated cases; this is a point of importance in distinguishing biliary from appendicular and intestinal colic where indican may be present.

Jaundice is not an invariable accompaniment of biliary colic. Its incidence has been variously estimated at one-half to three-quarters of all the cases. In the higher estimate cases of very slight and transient icterus are included. Naunyn § considers that definite jaundice is present in half the cases. It comes on a varying time after the onset of the pain, and no constant interval can be given. It may vary between a few hours to two or even three days. The occurrence of jaundice after biliary colic is the result of obstruction to the flow of bile through the common bile-duct. The obstruction is generally assumed to be due to the presence of the calculus in the duct, but it may be due to the spread of inflammation and spasm from the gall-bladder to the ducts, and may occur when the calculus is still in the gall-bladder or in the cystic duct. Riedel believes that two-fifths of the cases of jaundice in cholelithiasis are due to this cause.

As in other forms of jaundice, the urine contains bile-pigment before the conjunctivæ become stained, and the latter become yellow before the skin.

During an attack of gall-stone colic not only is no food taken, but the vomiting and fever lead to temporary loss of flesh and weight. When attacks are repeated, nutrition may become very seriously affected.

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* Kraus: On Gall-stones, p. 36, English translation, 1896.

† Ewing: Clinical Pathology of the Blood, p. 340.

‡ Gilbert and Weil: Soc. Méd. des Hôp., July 22, 1898.

§ Naunyn: Cholelithiasis, p. 76. Transl. New Sydenham Soc.

Complications.—The extremely forcible peristaltic contractions of the intestines, set up reflexly during the height of biliary colic, may lead to volvulus of the small intestine and so to acute intestinal obstruction. Mayo Robson * has drawn special attention to this complication of acute biliary colic. Intestinal obstruction produced by gall-stones in other ways, viz., by mechanical obstruction of the lumen of the bowel by a large calculus; as the result of local peritonitis around the gall-bladder, and by adhesions, is referred to elsewhere. (*Vide* pp. 742, 747, 749.)

Rupture of the gall-bladder or ducts during an attack is fortunately a very rare accident; when it occurs, infection of the peritoneum with fatal results is very prone to occur.

Pauly † describes a case in which, after an attack of biliary colic, collapse, abdominal distension, and death occurred. Blood clot was found in the abdomen. There was rupture of the capsule of the liver leading into a cavity containing blood. There were calculi in the gall-bladder and a calculus obstructing the common duct.

The cholecystitis which probably always precedes and gives rise to biliary colic may infect the peritoneum and set up peritonitis.

Termination.—An attack of biliary colic may terminate suddenly, the pain disappearing in a moment, probably from the calculus escaping into the duodenum. In other cases the pain may recur at frequent intervals, the calculus, or possibly a succession of calculi, being finally discharged into the duodenum. There does not appear to be any convincing evidence that recurrent attacks of colic without jaundice are due to a calculus which has once passed into the cystic duct, returning to the gall-bladder and entering the cystic duct again and again. Some of these cases are probably cholecystitis alone, while others may be due to pancreatic lithiasis.

In other instances the calculus may become impacted close to the biliary papilla and produce chronic jaundice and the symptoms of intermittent hepatic fever. (*Vide* p. 751.)

In rare instances death may occur from various causes. As has already been pointed out, the pain may be so intense that death results from reflex cardiac inhibition. Death from peritonitis due to rupture or ulceration of the ducts or gall-bladder is also described.

Diagnosis.—The extremely severe character of the pain in the right hypochondrium and back, the tenderness over the gall-bladder between the ninth costal cartilage and the umbilicus (Mayo Robson), vomiting, the subsequent development of jaundice, though this is not essential, and the recognition of gall-stones in the stools are the chief points on which a diagnosis of gall-stone colic rests. The presence of calculi in the fæces of course clinches the diagnosis, but calculi are by no means always found. To search for them the motions should be passed into a solution of carbolic acid 1 : 60, and broken up with the aid of a piece of stick and passed through a sieve.

The patient may be in such agony that it may be very difficult, especially in a first attack or when seen for the first time, to make out what is the matter. In such cases a hypodermic injection of morphia will relieve the patient to some extent and enable an investigation and a diagnosis to be made. A few whiffs of chloroform remove the widely spread pains and leave a subdued pain in the region of the gall-bladder.

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* Mayo Robson: Medico-Chirurg. Trans., vol. lxxviii, p. 117.

† Pauly: Lyon Médical, t. lxx, p. 430, July 24, 1892.

Differential Diagnosis from Cholecystitis.—In acute inflammation of the gall-bladder occurring in the absence of gall-stones the pain is less excruciating than when a calculus is impacted in the ducts. But, as already pointed out, Kehr * believes that cholecystitis is antecedent to every attack of biliary colic, and Naunyn † has shown how frequently cholecystitis accompanies biliary colic and how difficult it may be to distinguish between simple cholecystitis and biliary colic.

Renal Colic.—Since the pain due to a calculus in the cystic duct is felt to the right of the spine opposite the eighth to eleventh dorsal vertebræ, it is not surprising that cases of biliary colic are from time to time diagnosed as renal colic due to a calculus in the right kidney. In renal colic the pain tends to radiate down the ureter instead of forwards towards the epigastric and hypochondriac regions, while the kidney is tender on palpation in the loin, and the urine may contain blood, pus, or albumin, and is free from bile.

The diagnosis of cholelithiasis in early life is difficult, as it is hardly likely to be thought of unless there is jaundice. The abdominal pain will probably be referred to intestinal disturbance. In this respect cholelithiasis resembles renal colic in infants, which, as Gibbons ‡ has shown, is very likely to be overlooked.

Floating Kidney.—As described elsewhere (p. 546), a floating kidney on the right side may produce both biliary colic and jaundice. The diagnosis depends on the detection of a floating kidney and on disappearance of the symptoms when nephroptosis has been efficiently treated either by a belt and pad or by the operation of fixing the kidney in the loin (nephropexy). If attacks of jaundice and colic still continue, it is probable that there is cholelithiasis in addition, which is by no means infrequently the case.

Gastric and Duodenal Ulcer.—The pain due to biliary colic is often regarded not only by the sufferers, but also by their medical advisers, as due to disease of the stomach, such as ulcer, or as a duodenal ulcer. In some cases of biliary colic the pyloric end of the stomach may be involved in adhesions due to past attacks of local peritonitis originally set up by cholecystitis. In making a differential diagnosis it must be remembered that the pain of gastric ulcer has a direct relationship to food, while gall-stone pain frequently begins at night, hours after a meal has been taken, and when the stomach is empty. The pain of gall-stone colic is more to the right of the abdomen than that of gastric ulcer, and may be absent for long periods, while that of ulcer constantly recurs after food. In gastric ulcer the pain is chiefly in the epigastrium, and the vomited matters show excess of hydrochloric acid, while in biliary colic the amount of hydrochloric acid is either normal or diminished. Fever, sweating, rigors, and prostration are in favour of biliary colic.

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* Kehr: Gall-stone Disease, p. 26, American transl.

† Naunyn: On Cholelithiasis, pp. 113–125. Transl. New Sydenham Soc.

‡ Gibbons, R. A.: Med.-Chirurg. Trans., vol. lxxix, p. 41.

Acute Dyspepsia.—In acute gastritis with flatulent distension of the stomach the symptoms are less urgent than in biliary colic, and there is tenderness over the stomach rather than over the gall-bladder.

Hyperchlorhydria.—In some cases of nervous dyspepsia with hyperacidity of the gastric juice attacks of pain, which may wake the patient up at 3 in the morning, occur and may be regarded as due to biliary colic. Dr. T. McCrae has told me of such cases which, though very rare in England, are not so in America. Examination of the gastric juice and the relief obtained from bicarbonate of soda should enable the medical men to recognise the true nature of these cases.

Duodenal ulcer is very rare in women, and is often quite latent until it perforates into the peritoneal cavity, when it gives rise to symptoms. Pain comes on two hours after food, tenderness is to the right and much in the same position as the gall-bladder, and hæmatemesis may occur or there may be melæna without hæmatemesis.

Appendicitis.—In some cases the pain is referred to the right iliac fossa and the condition resembles appendicitis. A possible explanation of this is that local peritonitis has spread from the gall-bladder and involved the serous coat of the appendix (Tripier and Paviot *). In other words, it is the coëxistence of pericholecystitis with biliary colic which gives rise to the pain resembling that of appendicitis. Confusion is more likely to occur between ordinary cholecystitis and appendicitis than in typical biliary colic in which the pain is much more severe and higher up in the abdomen. It must also be remembered that in rare cases, of which Becker † has collected 34, appendicitis and cholelithiasis may coëxist.

Mucous Colic (or Colitis).—Occasionally the attacks of abdominal pain in mucous colitis are sufficiently severe to suggest the existence of biliary colic. Examination of the stools should lead to the detection of the characteristic casts, and so to a recognition of the real nature of the disease. It is worth while pointing out that membranous cholecystitis with attacks of biliary colic have been reported in patients with mucous colitis. (*Vide* p. 603.) Mucous colic may be associated with the passage of intestinal sand and with abdominal pain.

From Intestinal Lithiasis.—There are two forms of intestinal sand: (i) The false—or food residues, such as the sclerenchyma of fruits, especially the pips of pears, the vertebræ of sardines, or salts or drugs, such as magnesia or salol taken medicinally. It is important to be aware of the fact that olive oil taken by the mouth to relieve cholelithiasis may be passed as saponified masses, which, from a superficial or careless examination, may be regarded as softened calculi.‡ When colic from other causes, such as constipation, is followed by the passage of these food residues, a diagnosis of biliary sand might easily be made unless the masses are chemically or microscopically examined. (ii) True intestinal sand is composed of calcium phosphate, and is probably the result of a "lithogenic catarrh" of the intestine. It may also contain urobilin. The presence of true intestinal sand is often associated with mucous colitis. In some, but not in all, cases of true intestinal sand there are severe attacks of abdominal pain. A careful examination of the chemical nature of the sand is necessary to distinguish the condition from biliary colic due to minute calculi.

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* Tripier and Paviot: La Semaine Medicale, 1903, p. 29.
† Becker: Deutsch. Zeitschrift f. Chirurg., Bd. lxvi, S. 246.
‡ Compare Delépine, S.: Trans. Path. Soc., vol. xli, p. 111.

In acute pancreatitis there is more profound collapse; the pain is more in the epigastrium, and is more intense and constant than in biliary colic. Acute pancreatitis may follow on biliary colic (Thayer[*]), and the hæmorrhagic form may, as Opie[†] has shown, be due to bile passing into the pancreatic duct when the orifice of the biliary papilla is blocked by a small calculus.

Hepatic Crises in Tabes, etc.—Crises resembling biliary colic are very rare in tabes, but the resemblance may be very close, as is shown by the following case:

> Krauss[‡] records a case of a woman aged forty-four who was the subject of tabes and had recurring attacks of colic and jaundice. The autopsy showed that the gall-bladder and ducts were healthy and free from calculi. The liver showed chronic venous engorgement without any heart or lung disease to account for it. The condition was regarded as being analogous to gastric, renal, and other crises.

The obscure condition, hepatalgia, or neuralgia of the liver, has been described by Clifford Allbutt[§] and Pariser,[‖] the latter of whom has reported seven cases of nervous hepatic colic. The patients are neurotic or neurasthenic, but these conditions of course in no way protect against cholelithiasis. Osler[**] speaks of pseudobiliary colic as not uncommon in nervous women, and as being periodic and often excited by emotion, but not accompanied by jaundice. It may be difficult to exclude cholelithiasis completely, but the absence of jaundice is significant.

From enteralgia, or *neuralgia of the abdominal sympathetic*, the diagnosis is not always easy. According to Clifford Allbutt,[††] the pain of enteralgia often begins at the navel and is more stabbing than in biliary colic.

Pseudo-gall-stone colic may occur in malignant disease involving the ducts and in malignant disease of the head of the pancreas, but there is such deep jaundice and the condition of the patient is so grave that little or no difficulty in eliminating ordinary biliary colic is likely to arise.

Lead Colic.—In severe lead colic there is a superficial resemblance to gall-stone colic in that there are great abdominal pain and difficulty in making a thorough examination of the patient. The blue line on the gums, the anæmia, and the absence of any localisation of tenderness near the gall-bladder point to lead colic. I have seen recurrent attacks of colic with slight jaundice in a worker in lead, and the question arises whether spasmodic contraction of the bile-ducts may be set up by lead and be analogous to intestinal colic.

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[*] Thayer, W. S.: American Medicine, March 1, 1902.

[†] Opie, E.-L.: Johns Hopkins Hosp. Bull., 1901, vol. xii, p. 179.

[‡] Krauss: Journal of Nervous and Mental Diseases, vol. xxvi, p. 107, 1899.

[§] Clifford Allbutt: Visceral Neuroses, 1884, and his System of Medicine, vol. iii, p. 481.

[‖] Pariser: Centralblatt f. inn. Med., 1896, Bd. xvii, S. 467.

[**] Osler, W.: Practice of Med., p. 564, 4th ed., 1901.

[††] Clifford Allbutt: Allbutt's System of Medicine, vol. iii, p. 482.

Angina Pectoris.—The severity of the pain may, when it is referred to the cardiac region, lead to an erroneous diagnosis of angina pectoris; such cases, however, are very rare.

In a case of de Havilland Hall's[*] there were attacks of pain in the cardiac region, followed by faintness which resembled angina, but were not relieved by nitrites. Subsequently unmistakable biliary colic, followed by a broncho-biliary fistula, developed and the aberrant pain disappeared.

Lumbago.—The pain in the back with which biliary colic may begin may, in some cases, lead to an erroneous diagnosis of lumbago or of spinal disease unless a careful and complete examination is made.

Prognosis.—Under this heading recovery from the actual attack and the prospect as regards the future require consideration.

It is only in the rarest cases that death results during an attack of biliary colic. It may be due to the intensity of the pain giving rise to cardiac failure.

Naunyn[†] collected nine examples of this kind; Mayo Robson,[‡] Clifford Allbutt,[§] and Osler[‖] refer to other cases.

Death may be due to another cause, viz., rupture of the gall-bladder or bile-ducts during severe spasm, and perforative peritonitis due to the leakage of infected bile. Courvoisier[**] has collected 41 examples of this result.

In nearly all cases recovery takes place from the actual attack, but it is seldom that the first attack is the last. Usually there are a number of further attacks which are less severe than the first. As a rule, after a series of these attacks the patients become free from any further trouble. But a calculus is sometimes left in the common bile-duct and the symptoms of intermittent hepatic fever develop, or there is constantly recurring pain from the presence of adhesions around the gall-bladder (*vide* p. 749). The prognosis in some degree depends on the presence or absence of facets on a calculus found in the stools. If, after a first attack, a smooth gall-stone without any facets is found in the fæces, it may reasonably be hoped that no further attacks will follow. If, on the other hand, the calculus is facetted, there are other calculi in the gall-bladder and the probability of another attack must be faced. The patient's habit of life, his willingness or refusal to adopt means to avoid conditions which favour catarrhal cholecystitis and the production of fresh gall-stones, all bear on the prognosis.

Treatment.—The treatment of biliary colic consists in that of the painful paroxysm and of the patient during the intervals between the attacks.

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[*] de Havilland Hall: Lancet, 1902, vol. i, p. 593. Trans. Med. Soc., vol. xxv, p. 191.

[†] Naunyn: Cholelithiasis, p. 89. Transl. New Sydenham Soc.

[‡] Mayo Robson: Gall-stones, 1892, p. 77.

[§] Clifford Allbutt: System of Medicine, vol. iii, p. 471.

[‖] Osler, W.: Practice of Medicine, p. 565, 4th ed.

[**] Courvoisier: Beiträge z. Path. u. Chirurg. d. Gallenwege, 1890.

In *acute biliary colic* the pain is often so agonising that it will yield to nothing except hypodermic injections of morphia or inhalations of chloroform. After a hypodermic injection has been given, a few whiffs of chloroform will relieve the pain until the effect of the morphia makes the patient comfortable. One-fourth of a grain of morphia combined with $\frac{1}{100}$ grain of atropine may be injected in these cases, and if an inhalation of chloroform is not advisable, 20 minims of chloroform in water may be given by the mouth, as directed by Gilman Thompson.*

In a severe attack a hypodermic injection of morphia is very much better than opium by the mouth, both because it acts more rapidly and because the repeated vomiting which frequently accompanies severe biliary colic may lead to rejection of everything taken by the mouth. The hypodermic syringe should, of course, never be entrusted to the patient, as there is very considerable risk in cases where the attacks are frequently repeated of the morphia habit being acquired.

A short but graphic account of the intense suffering involved in breaking off the morphia habit acquired from repeated biliary colic is given by Keay in his book on the Medical Treatment of Gall-stones, p. 105.

Antipyrin, if given at the beginning of an attack, has been thought to give considerable relief. Kraus † considers that it does good chiefly by inducing profuse perspiration, and insists on its futility in cases where the attack has already lasted two to three hours and on the danger of collapse from its use.

Naunyn ‡ has had favourable results with a single dose of salicylate of soda (30–45 grains) given at the beginning of an attack. Some observers have found that copious draughts of warm water or several ounces of olive oil give relief, even though promptly vomited. In fact, providing fluid for the stomach to reject gives relief. Washing out the stomach has also been thought to alleviate the pain. (Baruch.§)

The vomiting accompanying the biliary colic hardly requires any special treatment apart from that of the pain, as it will cease with it. Bismuth, soda, dilute hydrocyanic acid, and iced apollinaris or soda-water may be given. Large draughts of water containing bicarbonate of soda (ʒj to Oj), recommended by Prout, relieve purposeless retching by giving the stomach something to bring up. If retching persists and the patient be collapsed, iced champagne may be given; otherwise it is better to give nothing by the mouth, to apply poultices to the epigastrium, and keep the patient under the influence of morphia administered hypodermically.

In less severe cases the patient may be put in a hot bath (104° F.) and given tincture of belladonna (♏xx) in spirits of chloroform to relieve spasm. Hot fomentations or poultices may be tried over the liver and antipyrin given by the mouth.

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* Gilman Thompson: Medical News (N. Y.), April 29, 1897.

† Kraus: On Gall-stones, p. 83. English translation, 1896.

‡ Naunyn: Cholelithiasis, p. 178. Transl. New Sydenham Soc.

§ Baruch: The Principles and Practice of Hydrotherapy, p. 235, 1900.

The external application of salicylate of methyl over the liver has been recommended in hepatic colic: a drachm to 2 drachms may be painted on daily and covered with gutta-percha to favour absorption. Chambart-Hénon * says it gives relief in half an hour.

Surgical Treatment.—During an attack of biliary colic operation is justified only in the presence of some severe complication which would otherwise prove fatal. These complications are (i) rupture of the gall-bladder or bile-ducts, with severe collapse and signs of perforative peritonitis; (ii) widespread peritonitis due to acute infective inflammation of the gall-bladder, and (iii) signs of acute intestinal obstruction due to volvulus of the intestine from exaggerated peristalsis.

When, in spite of medical treatment, attacks of colic continually recur and the patient becomes incapacitated and is in danger of contracting the morphia habit, surgical measures must be considered. The gall-bladder should be opened, calculi removed, and, if necessary, the gall-bladder itself removed, or Mayo's modified operation, removal of the mucous membrane, performed. Some difference of opinion has, perhaps naturally, existed between physicians and surgeons as to the recurrence of cholelithiasis after the operative removal of calculi from the gall-bladder. Keay,† in a vigourous plea in favour of the medical treatment of gall-stones, unhesitatingly states that recurrence occurs, and Homans ‡ and Kehr § have reported cases where fresh calculi formed around sutures introduced into the wall of the gall-bladder during an operation for the removal of calculi. Mayo,‖ from the surgeon's point of view, insists that *recurrence does not occur*.

It would appear, therefore, that when operation is required in recurrent biliary colic, the gall-bladder should either be removed or so treated that no fresh formation of gall-stones in it is possible. The treatment during the intervals is the general treatment of cholelithiasis described on page 763.

THE MECHANICAL EFFECTS OF GALL-STONES.

The purely mechanical effects of gall-stones will be considered seriatim under the following heads:

(1) In the gall-bladder.
(2) In the cystic duct.
(3) In the common bile-duct.
(4) In the ampulla of Vater.
(5) Intestinal obstruction.

(1) **Mechanical Effects of Gall-stones in the Gall-bladder.**—The mechanical effects pure and simple of calculi in the gall-bladder are not

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* Gaz. Méd. de Paris, 1898, p. 408.

† Keay: The Medical Treatment of Gall-stones, p. 96.

‡ Homans: Annals of Surgery, vol. xxvi, p. 114, 1897.

§ Kehr: Diagnosis of Gall-stone Disease, p. 105. American translation, 1901.

‖ Mayo: Boston Medical and Surgical Journ., vol. cxlviii, p. 545.

very frequent, or, as a rule, very important. A large calculous gall-bladder may give rise to a dragging sensation or feeling of heaviness and discomfort in the region of the liver.

The gall-bladder, when full of tightly packed calculi or containing a single large gall-stone, may exert pressure on the adjacent structures. By pressing on the pylorus or duodenum it may produce pyloric obstruction, dilatation of the stomach, and thus imitate carcinoma of the pylorus. (Naunyn,* Potherat.†) In these cases examination of the gastric contents may be of use in settling the diagnosis. Some free hydrochloric acid should be present in cholelithiasis, while in gastric carcinoma it should be absent. Gall-stones in the gall-bladder do not, as a rule, obstruct the outflow of food from the stomach simply and solely in a mechanical way, but set up adhesions between the pylorus and the gall-bladder (*vide* p. 749) which contract and slowly lead to pyloric obstruction.

In cases where a large single calculus is in process of ulcerating out of the gall-bladder into the duodenum, the calculus may mechanically obstruct the pylorus (*vide* Intestinal Obstruction Due to Gall-stones, p. 742). There may be a combination of cholecystogastric fistula, adhesions around the pylorus, and mechanical obstruction of the lumen of the pylorus by a calculus.

From the pressure of a large calculous gall-bladder the common bile-duct might be compressed and jaundice set up. Thrombosis of the portal vein from this cause has been reported.‡ From traction exerted by a heavy gall-bladder containing calculi the right lobe of the liver may be elongated into the formation known as a Riedel's lobe.

When the gall-bladder is filled with calculi, it may be felt as a hard tumor through the abdominal wall, sometimes just below the costal arch; in other cases, owing to the right lobe of the liver being elongated into the formation known as Riedel's lobe, the gall-bladder is considerably depressed and may be found in the neighbourhood of the right iliac fossa. Unless fixed by adhesions, the calculous gall-bladder moves with respiration and can be displaced in a lateral direction. When there are numerous calculi, a grating feeling of crepitus may be detected on palpation over the tumor, but this is often absent even when there are several calculi in the gall-bladder. A number of calculi may become loosely cemented together so as to form a large composite calculus which does not give rise to any crepitus and so resembles a large single calculus as big as a hen's egg. From absorption of bile the walls of the gall-bladder may become adherent to the surface of a contained calculus and be separated from it with difficulty.

When the gall-bladder is filled with a number of gall-stones and its walls are much atrophied, it is possible that spontaneous rupture may occur; but in most cases ulceration and softening due to inflammation must be regarded as the important antecedents of rupture of a gall-bladder containing calculi.

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* Naunyn: On Cholelithiasis, p. 151.

† Potherat: Soc. de Chirurg. Paris, June 10, 1903.

‡ Donkin: Medical Times and Gazette, 1868, vol. ii, p. 396.

The presence of calculi in the gall-bladder disposes to the development of primary carcinoma; this is perhaps the result of irritation rather than a purely mechanical effect, but until the causation of carcinoma is established, the rôle of gall-stones in the production of carcinoma of the gall-bladder must remain undecided. The association of cholelithiasis and primary carcinoma is discussed under Carcinoma of the Gall-bladder. (*Vide* p. 627.)

According to Schroeder, 14 per cent. of patients with cholelithiasis eventually develop carcinoma of the gall-bladder. In 149 cases of gall-stones examined at Guy's Hospital there were 17, or 11 per cent., of cases of primary carcinoma of the gall-bladder (Keay *). Among 242 cases of gall-stones at St. George's Hospital there were 10 cases of primary carcinoma of the gall-bladder, or 4.1 per cent.

(2) **Mechanical Effects of Calculi in the Cystic Duct.**—When a calculus passes into the cystic duct, it stretches the walls and sets up spasm and biliary colic. (*Vide* p. 723.) A calculus may remain impacted in the cystic duct for long periods; sometimes no definite history of past colic is forthcoming in such cases to mark the time of impaction. The calculus is nearly always fixed close to the neck of the gall-bladder. It may completely obstruct the flow of bile into the gall-bladder, which then becomes distended with mucus, at first mixed with bile, but later quite clear. This is hydrops vesicæ felleæ, or dropsy of the gall-bladder. Infection and cholecystitis are very prone to occur under these conditions. The distended gall-bladder may be the site of painful spasmodic contractions resembling biliary colic in their clinical aspect, except that jaundice is usually absent; in some of these cases the condition is very likely to be regarded as indigestion. Jaundice may, however, be brought about by extension of spasm to, or by concomitant catarrhal inflammation of, the common bile-duct. According to Riedel,† jaundice is present in from 10 to 15 per cent. of the cases where a calculus is impacted at the neck of the gall-bladder. Attacks of painful spasm in a distended gall-bladder have been explained as depending on a calculus in the neck of the gall-bladder acting as a valve and allowing bile to enter the gall-bladder but not to leave it. It is, however, more probable that the distension of the gall-bladder is not purely mechanical and due to a valvular action of a calculus, but that there is inflammation of the mucous membrane of the gall-bladder, which accounts for both the distension and the pain.

A *distended gall-bladder* appears as an abdominal tumor in the right half of the abdomen; in very rare instances it is so large as to occupy the greater part of the abdomen, and has been mistaken for ascites and tapped. Usually it is not larger than one's closed fist. The dilated gall-bladder may be associated with an elongated condition of the right lobe of the liver, Riedel's linguiform lobe, and as a result the gall-bladder may form a tumor in the right iliac fossa and might imitate appendicitis.

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* Keay: The Medical Treatment of Gall-stones, p. 67.

† Riedel: Berlin. klin. Wochen., Jan. 21, 1901, S. 78.

H. J. Waring * figures a gall-bladder which entered into a right femoral hernia. It forms a smooth, tense, pear-shaped tumor with the apex upwards and the base downwards. It usually moves with respiration and can be displaced laterally, but not downwards. It is separated from the liver by a groove or depression, is immediately under the abdominal walls, and in thin patients may be visible as a raised surface. It is not tender unless there is concomitant inflammation. It may be resonant on percussion. A gall-bladder which has been distended with mucus from obstruction of the cystic duct may subsequently shrivel up and become very contracted.

A distended gall-bladder must be distinguished from a floating kidney, a renal tumor or hydronephrosis, a tumor of the pylorus, a growth in the transverse colon, etc. Confusion is most likely to arise between a distended gall-bladder and a floating kidney on the right side, since they are both commoner in women and may both be accompanied by attacks of severe pain followed by jaundice. An enlarged gall-bladder forms a tumor which is much more constant and does not disappear or vary in position in the same way as a floating kidney. A gall-bladder is usually movable, but is limited by its attachment to the liver and cannot be displaced into the false pelvis like a floating kidney. If displaced backwards towards the loin, it returns to its former position directly the pressure is removed, while a floating kidney tends to remain there as long as the patient is in the recumbent position.

A distended gall-bladder does not escape from one's grasp in the same way that a floating kidney does. A careful bimanual examination should always be made. Morris † points out that too much stress is apt to be laid on hollowness and diminished resistance in the loin as signs of floating kidney.

Distension of the colon with air (Ziemssen's test) may be useful, as it should press the gall-bladder forwards and displace a floating kidney backwards; but it is not infallible. Mayo Robson met with a case in which it pushed a growth of the right suprarenal body forwards. Kehr also distrusts this test, as the colon may pass in front of the gall-bladder. In a fat person it may be very difficult to be certain whether one is dealing with a floating kidney or a distended gall-bladder, and in such cases an exploratory operation may be the only means of settling the diagnosis. In some cases a floating kidney and a distended gall-bladder may both be present.

Chance ‡ described a case of a dilated gall-bladder containing 200 calculi which exactly imitated a tuberculous kidney.

A tumor of the pylorus lies in a plane, roughly speaking, at right angles to that of the gall-bladder and is harder and painful. In gall-bladder cases there may be gastric symptoms and some dilatation of the stomach from pyloric obstruction, but the gastric symptoms are not so

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* Waring, H. J.: Diseases of the Liver, p. 235.

† Morris, H.: Brit. Med. Journ., 1895, vol. i, p. 238.

‡ Chance: Medical Chronicle, vol. xxxvii, p. 120, Nov., 1902.

prominent as in pyloric new-growth. A tumor of the transverse colon is less sharply defined than a dilated gall-bladder, and, like the pyloric tumor, tends to have its long axis at right angles to that of a distended gall-bladder. Fæcal impaction in the transverse colon will usually be accompanied by fæcal masses elsewhere in the abdomen, and the condition will be cleared up or altered by the use of enemata. It may be impossible to distinguish between a small dependent hydatid cyst and a dilated gall-bladder until the abdomen is opened. Aspiration would probably settle the matter, but this is too dangerous a method to be recommended.

In a woman aged forty a dilated gall-bladder containing eleven pints of liquid, due to a calculus impacted in the cystic duct, imitated a parovarian cyst. (L. Tait.*)

Naunyn † quotes two cases in which a calculus in the cystic duct exerted direct pressure—on the portal vein in one instance, and on one of its branches in the other—and set up pylethrombosis. Hæmatemesis may thus be an indirect result of cholelithiasis. A calculus in the cystic duct may possibly exert pressure on the common hepatic duct and so give rise to jaundice.

The passage of calculi along the cystic duct leads to dilatation and to straightening out of the tortuous lumen of the duct, and so facilitates the subsequent passage of calculi from the gall-bladder. The valves of Heister, which under ordinary conditions obstruct the return of a calculus from the duct into the gall-bladder, become almost obliterated and only appear as slight elevations of the mucous membrane; when thus altered, they may allow a calculus to travel towards the gall-bladder.

In a case under my care a large gall-stone in the common duct was displaced at a laparotomy, undertaken for its removal, by manipulation, and was thought to have passed into the duodenum. At the autopsy, however, it was found in the gall-bladder.

(3) **Mechanical Effects of Gall-stones in the Common Bile-duct.**—The passage of a calculus through the common bile-duct sets up biliary colic. (*Vide* p. 723.) A calculus may, however, pass into the common duct and become permanently lodged there without giving rise to the symptoms of colic.

Situation of the Calculi in the Common Duct.—Statistics vary as to the commonest site for a calculus. The general impression is that the termination of the duct in the biliary papilla and the ampulla Vateri are the commonest situations for calculi.

Courvoisier's statistics bear this out: in 123 observations the calculi were found to occupy the whole of the common bile-duct in 26; the upper segment in 17; the middle segment in 19; to be close to the duodenum in 20; in the orifice of the biliary papilla in 41; so that in almost exactly half the cases the calculus was close to the lower end of the duct. In 380 operation cases Mayo Robson ‡ found the calculus in the duodenal end in 67 per cent., in the middle portion in 18 per cent., and at the upper end in 15 per cent.

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* Lancet, 1889, vol. i, p. 1294.

† Naunyn: Cholelithiasis, p. 133. Transl. New Sydenham Soc.

‡ Mayo Robson: Diseases of the Gall-bladder and Bile-ducts, p. 278, 1904

In a smaller number of cases Vautrin * comes to the opposite conclusion: number of cases, 47; calculi in part of the duct above the duodenum, 27; in part of duct in contact with the duodenum, 18; in the ampulla Vateri, 2. This distribution he explained by the fact that the duct is readily dilatable above the duodenum, but resists dilatation where it is supported by the pancreas.

Number of Calculi in the Common Duct.—In the great majority of cases there is a single calculus; thus in 149 observations Courvoisier † found that in 95 there was a single calculus, in 36 instances there were from two to six calculi, and in the remaining 18 there were a dozen or more calculi in the duct. A single calculus is usually firm, but there may be a soft, crumbling mass which fills up the whole of the dilated duct and may extend into the common hepatic duct. Several soft crumbling calculi may be found. Mayo Robson has removed 88 calculi from the common duct.

In very rare instances a calculus in the common bile-duct may mechanically compress the portal vein and give rise to thrombosis. Cases of this nature have been reported by Naunyn,‡ Westenhoffer,§ Körte.‖

It is possible that the reflex irritation of calculi in the common duct, quite apart from catarrh, may give rise to vomiting. Leclerc ** reports a case in which vomiting persisted for forty days until two calculi were removed from the common duct; there was no cause, such as adhesions or pyloric obstruction, for the vomiting.

A calculus may completely obstruct the common duct, partially occlude the lumen so that some bile can run past it into the duodenum, or be floating in the common duct and exert a ball-valve action. A calculus which at first is firmly impacted and completely occludes the common duct may subsequently become loose. This is due to several factors: the obstruction dilates the ducts above and thus leads to widening of the duct at the point of impaction; the constant pressure of the calculus produces atrophy of the walls of the common duct, while inflammatory softening and ulceration are extremely likely to occur. It is, therefore, rare for absolute biliary obstruction to persist for a long time, but jaundice may be kept up both from intermittent obstruction depending on the ball-valve action of a calculus described by Osler †† and by Fenger,‡‡ and also from concomitant inflammation of the bile-ducts—either the larger extra-hepatic or the small intra-hepatic.

Jaundice which has been marked early in the course of the impaction may wane and finally disappear, and after death a loose calculus may be found in the duct.

Griffon §§ records 4 cases of this kind where the calculus was found just above the biliary papilla.

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* Vautrin: Rev. de Chirurg., 1896, p. 454.
† Courvoisier: Path. u. Chir. d. Gallenwege, 1890.
‡ Naunyn: Cholelithiasis, p. 133. Transl. New Sydenham Soc.
§ Westenhoffer: La Semaine Médicale, 1903, p. 33.
‖ Körte: Ibid.
** Leclerc: Lyon Médical, tome c, p. 737.
†† Osler, W.: Med. Times and Gaz., July 31, 1881.
‡‡ Fenger, C.: American Journ. of Med. Sciences, vol. cxi, p. 125, 1896.
§§ Griffon: Bull. Soc. Anat., July, 1896, p. 513.

Chronic obstruction of the bile-duct with calculi may, however, induce long-standing jaundice. In these cases there may be a large crumbling calculous mass occupying a considerable extent of the common bile-duct. A calculous accumulation of this kind grows from deposit of bilirubin-calcium and is accompanied by infective cholangitis. When the duct contains a single calculus, jaundice, though present for a time, usually passes away.

As the result of obstruction of the common duct by calculi there may be—(i) Cylindrical or (ii) saccular dilatation of the duct.

(i) *Cylindrical dilatation* of the common bile-duct is the commoner. The duct is not infrequently the size of a test-tube, and may be larger and become comparable to a piece of intestine. The cylindrical dilatation may spread through the common and hepatic ducts into the liver and give rise to dilatation of the intra-hepatic bile-ducts. The dilatation is more marked on the surface of the organ, and is often more prominent in the left lobe, probably because there is less resistance on the surface of the liver and especially in the smaller left lobe. Local saccular dilatations of the varicose bile-ducts on the surface of the liver may occur.

(ii) *Saccular Dilatation.*—In rare instances the common bile-duct may form a large cyst which may be diagnosed as a dilated gall-bladder, a pancreatic cyst, a hydatid cyst, etc. The condition is like that described on page 651. Occasionally there are local cystic dilatations in the intrahepatic branches of the bile-ducts on the surface of the liver; this local dilatation may be superimposed on a widespread cylindrical dilatation.

Simply from distension with bile *the liver* becomes at first enlarged. Subsequently atrophy of the liver cells occurs, with prominence of the existing fibrous tissue. The question whether mere stasis of the bile can lead to genuine hepatic cirrhosis has given rise to considerable discussion (*vide* p. 329) and experimental investigation. The conclusions from human morbid anatomy are that biliary obstruction alone does not induce real cirrhosis, but if infection of the bile-ducts occurs, pericholangitic fibrosis will result. In obstruction of the ducts with calculi infective cholangitis is readily produced, and thus fibrosis of the liver may result.

(4) **The Mechanical Effects of a Calculus in the Ampulla of Vater.**—An important difference between the mechanical effects of a calculus in this situation and of one in the lower end of the bile-duct is that when the calculus occupies the ampulla of Vater, it may in addition obstruct the outflow of pancreatic juice from Wirsung's duct. The accessory duct of Santorini may, however, carry off the secretion into the duodenum, and so prevent any accumulation of the pancreatic juice in the ducts. In about one-third of the cases, however (Schirmer *), there is no communication between the two ducts, and in these cases obstruction of the orifice of Wirsung's duct would lead to its distension with pancreatic secretion.

As a matter of fact, however, there is nearly always some additional inflammatory change when a calculus is in the ampulla of Vater. This sets up pancreatitis and leads to enlargement and fibrosis of the pancreas, dilatation of Wirsung's duct, and in some instances to the formation of pancreatic calculi. The chronic interstitial pancreatitis which results from obstruction of the ducts hardly ever destroys the islands of Langerhans, and hence glycosuria and diabetes do not result. (Opie.[*])

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* Schirmer: Inaug. Dissert., Basel. Quoted by Opie: Amer. Jour. Med. Sci., vol. cxxi, p. 30.

When a small calculus is impacted in the ampulla of Vater close to the biliary papilla and is not sufficiently large to obstruct the opening of the main duct of the pancreas into the ampulla Vateri, the direct mechanical obstruction to the flow of bile into the duodenum results in the passage of bile into the pancreatic duct. This has been shown by Halsted and Opie [†] to have occurred in a fatal case of hæmorrhagic pancreatitis. Opie has, moreover, proved by experiments on dogs that the passage of bile into the pancreatic duct induces hæmorrhagic pancreatitis. The reason why impacted calculi in the diverticulum of Vater only rarely induce hæmorrhagic pancreatitis is that usually the calculi are sufficiently large to obstruct the orifice of Wirsung's duct and so interfere with the entrance of bile into the pancreatic duct.

(5) **Mechanical Obstruction of the Intestines by Gall-stones.**—*Incidence.*—When a large gall-stone ulcerates out of the gall-bladder into the duodenum, or in rare instances into the colon, it may produce mechanical obstruction of the bowel. This is a decidedly rare event in ordinary practice, as is shown by the fact that at the Leeds Infirmary, where a large number of gall-stone operations are done, only one case has occurred in ten years.[‡] Only one case occurred at St. George's Hospital in fifteen years. But from the interest attaching to such rare and striking cases a large number have been reported, and Morestin,[§] in 1900, was able to refer to as many as 242 cases. The relative frequency of this cause to other causes of intestinal obstruction has been variously estimated at from 1 to 13 to 1 to 45.

In 295 cases of intestinal obstruction Fitz found 23 due to gall-stones, or 1 in 13; Gibson,[‖] 40 in 696, or 1 in 17; Leichtenstein, 41 in 1152, or 1 in 28; while in 360 consecutive cases of intestinal obstruction in eight years at the London Hospital Barnard [**] found 8, or 1 in 45, due to gall-stones.

Entrance of the Calculus into the Intestine.—It is probably very seldom that a calculus which passes down the bile-duct into the duodenum is of sufficient size to occlude mechanically the ileocæcal valve. In some instances a large calculus is found projecting from the lower end of the bile-duct, and it is conceivable that such a calculus, after squeezing through the biliary papilla into the duodenum, would be large enough to obstruct the ileocæcal valve. Most writers, however, are agreed that a calculus which passes down the common bile-duct into the duodenum is hardly ever large enough to obstruct the intestine mechanically. It is probable that a comparatively small calculus, after passing into the intestine, may increase in size from addition of phosphates to its surface, as in Eve's case,[*] and so become large enough to cause obstruction in the ileum or ileocæcal valve. Treves [†] removed a calculus, with a diameter in its long axis of 1½ inches, from the ileum of an old lady who for years had taken carbonate of magnesia daily. Its nucleus was a small gall-stone, and its large size was due to layers of magnesia and fæcal material.

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[*] Opie, E. L.: Jour. Exper. Med., vol. v, p. 397, 1901.

[†] Halsted and Opie: Johns Hopkins Hospital Bull., vol. xii, Nos. 121, 122, 123, April, May, June, 1901.

[‡] *Vide* Moynihan: Medical Chronicle, vol. xxxviii, p. 277, 1903.

[§] Morestin: Bull. Soc. Anat. Paris, 1900, p. 196.

[‖] Gibson, C. L.: Annals of Surgery, October, 1900, p. 506.

[**] Barnard, H. L.: Annals of Surgery, Aug., 1902, p. 161.

In other and very rare instances intestinal obstruction may be due to impaction of a congeries of small calculi in the intestine (Cantlie[‡]). A calculus which is not sufficiently large to obstruct the normal small intestine may, if the intestine is narrowed from some other cause, completely obstruct the stricture.

Thus Mayo Robson [§] found a calculus entangled in a pouch between two tuberculous strictures of the ileum. Garrett [‖] found a gall-stone arrested just above a point where the small intestine passed under an omental cord; the bowel was thus completely occluded.

A comparatively small calculus may, especially if it is angular, set up spasm of the intestinal wall around the calculus, and so lead to closure of the lumen of the bowel; this theory explains the fact that in some fatal cases of gall-stone obstruction the calculus has been found loose in the bowel. Another method by which a comparatively small calculus may cause intestinal obstruction is by setting up localised inflammation of the mucous membrane of the bowel in its immediate neighbourhood. The resulting swelling and spasm of the wall of the bowel may then lead to impaction of the calculus.

In the vast majority of cases mechanical obstruction of the intestine by gall-stones is due to a large calculus which has ulcerated out of the gall-bladder into the duodenum, or less commonly into the transverse colon. Intestinal obstruction is much more likely to follow the passage of a calculus into the duodenum, as it has then to pass through the duodenum, jejunum, and the narrowed lower part of the ileum, than in cases where a calculus ulcerates directly from the gall-bladder into the colon.

It is a curious fact that a calculus may enter the intestine and remain there comparatively quietly for days, months, or even years, and yet eventually give rise to intestinal obstruction. When a calculus is in the intestine, it may give rise to repeated attacks of colic, vomiting, and pain, suggesting mild obstruction, and finally bring about acute obstruction.

In Sir T. Smith's [**] case the calculus was thought to have entered the intestine fifteen years before acute obstruction was produced.

As there may be two calculi in the intestine, attacks of transient obstruction may recur even after a calculus has been passed by the bowel.

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[*] Eve, F.: Trans. Clinic. Soc., vol. xxviii, p. 91.

[†] Treves, F.: Intestinal Obstruction, p. 193, 2d ed., 1899.

[‡] Cantlie, J.: Brit. Med. Jour., 1904, vol. i, p. 181.

[§] Mayo Robson: Trans. Clin. Soc., vol. xxxv, p. 58.

[‖] Garrett: Brit. Med. Journ., 1902, vol. ii, p. 789.

[**] Lancet, Dec. 3, 1887.

As already pointed out, there may be a want of proportion between the size of the gall-stone and the intestinal manifestations produced by it. Thus a comparatively small but angular calculus may set up so much spasm that the symptoms of obstruction are produced, while a smooth calculus of much larger dimensions may be passed by the rectum with little pain.

It is probable that all large calculi spontaneously passed by the bowel have entered the transverse colon from the gall-bladder by a cholecysto-colic fistula, for a calculus with a diameter of an inch or more would almost certainly become impacted at the ileocæcal valve. Among Gibson's * 40 cases the largest gall-stone weighed three and one-half ounces.

Site of the Obstruction.—The obstruction is most frequent in the lower end of the ileum near the ileocæcal valve. When a large calculus ulcerates from the gall-bladder into the duodenum, the site of the obstruction may be in the duodenum itself, at its junction with the jejunum, or in the ileum. When a calculus ulcerates into the colon, the obstruction may occur in the sigmoid flexure or close to the anus.

In 53 cases Courvoisier † found the site of obstruction to be in the ileum in 65.4 per cent.; in the duodenum, 21.4 per cent.; at the ileocæcal valve, 10 per cent., and in the sigmoid flexure, 2.4 per cent. In 40 cases collected by Gibson ‡ the calculus was impacted in the large intestine in one case only; in the ileocæcal valve in one instance, and in all the other cases in the small intestine.

Sex.—Intestinal obstruction due to gall-stones is very much commoner in women than in men. This is a natural result of the great frequency of cholelithiasis in women.

In Naunyn's 127 cases 34 were men and 93 women. In 50 recent cases which I have collected there were 42 females and 8 males.

The average age is over fifty years of age. In 50 recent cases the average age was 62.7 years, and many cases between 70 and 80 years of age have been reported.

Clinical Picture.—The onset is sudden. In some cases it has been preceded by attacks of vomiting and pain, but usually signs suggesting that the calculus has been for some time in the bowel are absent, and there may be no evidence of former gall-bladder trouble or of cholelithiasis. In 41 out of 120 cases the onset was preceded by symptoms which could be referred to ulceration of the calculus into the intestine. (Naunyn.) Although the bowel is obstructed, it is not strangulated, and as the circulation through its walls is not interfered with, they do not become paralysed and hence tympanites is usually absent, while flatus and fæces are often passed by the bowel. A calculus has been known to ulcerate out of the bowel and set up peritonitis.§ At first pain and collapse are not marked. Vomiting is usually an early symptom, and when the calculus is impacted in the duodenum or in the upper part of the small intestine, the vomited matter is bilious and does not become stercoraceous. It may contain blood from hæmorrhage produced in the process of ulceration of the calculus into the duodenum.

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* Gibson: Annals of Surgery, Oct., 1900, p. 506.

† Courvoisier: Patholog. u. Chirurg. der Gallenwege, 1900.

‡ Gibson, C. L.: Annals of Surgery, Oct., 1900, p. 506.

§ Jeaffreson: Brit. Med. Jour., 1868, vol. i, p. 531.

The impaction may persist, so that unless relieved by operation death occurs from acute obstruction; in about 50 per cent. the symptoms are spontaneously relieved, sometimes quite suddenly, so that the patient at once knows that his condition has improved. In some instances, even though the patient has been relieved from the acute symptoms of obstruction, the wall of the bowel is so damaged that perforation or leakage from an ulcer occurs and sets up peritonitis.

Duration and Prognosis.—In fatal cases death usually occurs within five to ten days after the onset from collapse. In Sands' case * recovery took place after the condition had lasted for twenty-eight days; this is the longest case on record. About 50 per cent. of the cases die if not operated upon. The statistics of cases operated upon show a high mortality; thus in Schuller's 82 cases there was 56 per cent.; in J. Hutchinson's (Sr.), 50 per cent.; and in Courvoisier's 125 cases of operation, 44 per cent., of deaths.

Diagnosis.—When there is a definite history of gall-stones in the past and acute obstruction comes on suddenly with the presence of a hard, rounded tumor in the abdomen, the diagnosis would appear to be fairly clear. But, unfortunately, in a number of the cases there is no definite history of cholelithiasis, and the gall-stone is hardly ever felt in the abdomen before the operation.

In two cases reported by Barnard † the calculus was felt before operation.

It is possible that examination under an anæsthetic might enable a calculus to be felt in a certain number of cases. But as a matter of fact, the condition is very seldom correctly diagnosed before the abdomen is opened or the calculus is spontaneously passed by the rectum.

Treatment.—As the symptoms are those of intestinal obstruction and it is seldom possible to make a certain diagnosis of mechanical obstruction of the intestine by a gall-stone, the safest course is to open the abdomen and remove the stone by incising the bowel. In cases where the stone is comparatively small and is impacted at the lower end of the ileum, it might be pressed on into the colon. It is important that if an operation is necessary, it should be undertaken as soon as possible, for the patients are usually elderly and are often wanting in vitality.

Medical treatment has been successful in a certain number of cases. The most reasonable method seems to be to give belladonna or atropine in order to relieve spasm, and so to allow of the onward passage of the calculus; this method should be adopted in less severe cases in which there is any reason to suspect or believe that the cause of obstruction is an impacted calculus in the intestine, and at an early stage. In such cases Mayo Robson ‡ advises morphia to relieve the pain, and extract of belladonna (¼ gr.) every four hours, while chloroform anæsthesia may be of use in two ways—by allowing a thorough examination of the abdomen, by which the diagnosis may be cleared up if it is doubtful, and possibly by allowing manipulation to reduce or remove the obstruction. If these measures fail, operation should be undertaken without further delay.

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* Quoted by Treves: Intestinal Obstruction, 2d ed., p. 388.
† Barnard, H. L.: Annals of Surgery, Aug., 1902, p. 161.
‡ Mayo Robson: Diseases of the Gall-bladder and Bile-ducts, p. 157, 1904.

J. Hutchinson * has advocated a policy of surgical non-interference in cases of gall-stone obstruction, and has urged the use of anæsthetics, opium, and rectal injections with air or fluid to diminish spasm and assist in the passage of the calculus. Massage has been known to lead to a cure.

Treves † quotes a case of Martin's ‡ in which massage was employed on the sixth day of obstruction and on the next day a large gall-stone and ten smaller stones were evacuated.

INFLAMMATORY AND INFECTIVE CHANGES SET UP BY GALL-STONES.

The inflammatory and infective changes due to gall-stones include a large number of the irregular symptoms of cholelithiasis, and will be conveniently described under the various headings of changes in connexion with —(A) The gall-bladder; (B) the cystic, and (C) the common bile-duct and ampulla of Vater; while an account of the various fistulæ due to cholelithiasis will be given.

SYNOPSIS.

- (A) Gall-bladder:
  - Cholecystitis.
  - Ulceration.
  - Hæmorrhage.
  - Scars; hour-glass contraction.
  - Perforation; fistulæ.
  - Pericholecystic adhesions to pylorus, duodenum, colon, etc.
- (B) Cystic duct:
  - Swelling.
  - Obliteration.
  - Diverticulum.
- (C) Common bile-duct and ampulla of Vater:
  - Intermittent hepatic fever.
  - Extension to pancreatic duct—pancreatitis; cysts.
  - Extension to portal vein—pylephlebitis.
- Fistulæ.

(A) **Inflammatory and Infective Changes in the Gall-bladder.**—Although gall-stones are due to inflammation, of a comparatively mild character, of the gall-bladder, their presence disposes to fresh infection of the gall-bladder and thus to cholecystitis and to a vicious circle.

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* Hutchinson, J.: Archives of Surgery, April, 1896.

† Treves: Intestinal Obstruction, p. 467, 2d ed., 1899.

‡ Martin: Bull. Soc. Anat. Paris, 1875, p. 195.

Mieczkowski,* from examination of the bile of 15 patients whose gall-bladders were healthy and were extirpated during laparotomy for other conditions, concludes that human bile is sterile. In 23 cases of cholelithiasis investigated by him the bile was infected in 18. Gall-bladders containing gall-stones, therefore, are usually infected and are thus prone to fresh attacks of cholecystitis.

Cholecystitis.—Inflammation of various degrees of severity may supervene in a gall-bladder containing gall-stones. There may be acute infective cholecystitis, serous, serofibrinous, or purulent, which may go on to ulceration and perforation or gangrene; or there may be chronic serous or purulent cholecystitis; the latter condition is often spoken of as empyema of the gall-bladder. Descriptions of these various forms of cholecystitis are given elsewhere. (*Vide* p. 596.)

Acute cholecystitis may set up local peritonitis, and by paralysing the peristaltic movements of the intestines, may imitate acute intestinal obstruction.

Ulceration of the mucous membrane of the gall-bladder may give rise to: (1) Changes in the gall-bladder—(*a*) Hæmorrhage. (*b*) Scars. (*c*) Hour-glass contraction and diverticula. (2) Perforation of the gall-bladder: (*a*) Into the general cavity of the peritoneum. (*b*) Into part of the peritoneum shut off by adhesions. (*c*) Into the duodenum, colon, etc. (*vide* Fistulæ, p. 756). (*d*) Into other adjacent structures, such as bile-ducts, portal vein, hepatic artery. (*e*) Into the liver.

(*a*) *Hæmorrhage.*—As the result of an ulcer due to cholecystitis hæmorrhage may take place into the gall-bladder. This may depend on erosion of a small vessel in the wall of the gall-bladder, but in rare instances ulceration of the gall-bladder may involve the trunk of the hepatic artery and give rise to the formation of an aneurysm (*vide* p. 43) which may subsequently rupture.

(*b*) *Scars.*—As a result of the healing of an ulcer in the mucous membrane of the gall-bladder a scar results. In 343 cases of cholelithiasis tabulated by Schloth † there were 14 with cicatrices. These are more commonly seen at the fundus or close to the origin of the cystic duct. Their site depends to some extent on the mechanical irritation of the calculus. It may be pointed out, however, that what looks like a scar on the surface of the gall-bladder may in reality be a very early stage of primary carcinoma of the gall-bladder.

(*c*) *Hour-glass Contraction.*—Cicatrisation following inflammation and ulceration may lead to the production of hour-glass contraction of the gall-bladder. The gall-bladder may thus become divided into two compartments which communicate by a narrow channel. One or both of these two divisions may contain calculi. The communication between the two may become impervious, so that the fundus no longer communicates with the cystic duct.

Kehr ‡ records such a case in which one compartment contained pus, the other clear bile. In Donald's § case the peripheral part only contained mucus.

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* Mieczkowski: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1900, Bd. vi. Abstract in American Journ. Med. Sciences, 1902, vol. cxxiii, p. 372.

† Schloth: Diss., Wurzburg, 1887. Quoted by Naunyn.

‡ Kehr: Diagnosis of Gall-stone Disease. American translation, p. 48.

§ Donald: Glasgow Medical Journ., 1898, p. 348.

Courvoisier collected 15 examples of hour-glass gall-bladder, and others have been recorded since his monograph was published in 1890. Much the same kind of change is in progress in cases where a number of septa spring from the walls of the gall-bladder and form ridges between a succession of calculi. In this way the gall-bladder may become divided into a number of loculi or compartments communicating by narrow orifices.

H. L. Barnard * described a case where the gall-bladder contained four such compartments, one of which opened into the duodenum.

(2) *Perforation of the Gall-bladder.*—(*a*) *Into the General Cavity of the Peritoneum.*—When perforation or rupture of an inflamed gall-bladder takes place and the general cavity of the peritoneum is not shut off by old or recent adhesions, the bile and even gall-stones pass into the peritoneum and set up severe and usually fatal peritonitis. This is seen in cases of phlegmonous and gangrenous cholecystitis (*vide* pp. 610 and 612).

(*b*) *Into a Localised Pocket of the Peritoneum Cut off by Adhesions.*—A local abscess formed in connexion with perforation of a calculous gall-bladder into part of the peritoneum previously cut off by adhesions may contain gall-stones, and may open in one or more of a number of different situations, such as the duodenum, stomach, on the surface of the abdomen, etc. (*vide* Biliary Fistulæ), or present as a subphrenic abscess, or give rise to an empyema on the right side.

(*c*) *Ulceration of the Gall-bladder into the Substance of the Liver.*—Ulceration of the gall-bladder may extend directly into the substance of the liver; it may then give rise to an abscess cavity in the liver communicating with the gall-bladder, or to hæmorrhage into the gall-bladder.

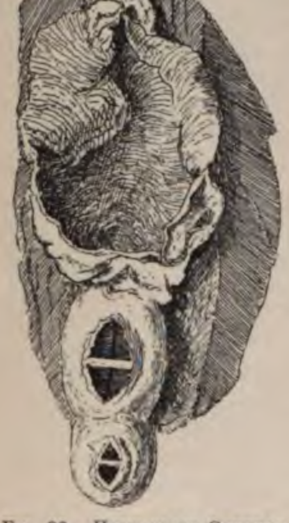

FIG. 96.—HOUR-GLASS CONTRACTION OF GALL-BLADDER.

The fundus, which communicates with the remainder of the gall-bladder through a minute orifice admitting a bristle, contains two calculi, one above the other, partially separated from each other by a septum from the wall of the gall-bladder. (Drawn by Dr. G. H. Goldsmith.)

Arbuthnot Lane † described a case where an encysted cavity in the liver, which contained calculi, opened into the gall-bladder; and a second case‡ in which rupture of the gall-bladder, which probably contained a calculus, on its anterior surface, extended into the substance of the liver and gave rise to profuse hæmorrhage into the gall-bladder.

This, however, is a very rare event.

(*d*) Ulceration of the gall-bladder may extend into the common bile-ducts, portal vein, and hepatic artery in the lesser omentum. These events are also referred to under the head of biliary fistulæ (*vide* p. 756): they are very rare. Ulceration of the hepatic artery may give rise to the production of an aneurysm (*vide* p. 43).

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* Barnard, H. L.: Annals of Surgery, Aug., 1902, p. 161.

† Lancet, 1893, vol. ii, p. 874.

‡ Trans. Clinic. Soc., vol. xxviii, p. 160.

Ulceration of the gall-bladder with the formation of fistulæ in connexion with various internal organs and with the outside of the body is dealt with below (*vide* p. 756).

Pericholecystic Adhesions.—As the result of inflammation around the gall-bladder adhesions readily form and unite it to adjacent organs, especially the pyloric end of the stomach or the duodenum. According to the thickness and density of the adhesions symptoms of a varying degree of intensity are induced. In the slighter cases there is pain after food, or "adhesion dyspepsia" due to interference with the gastric movements and to dragging on adhesions. These cases come under observation as indigestion or gastralgia, and imitate "adhesion dyspepsia" due to the effects of a past gastric ulcer. When the adhesions are firmer and dense, the pylorus or the duodenum may be so constricted or kinked that pyloric obstruction is induced, and the case may closely resemble carcinoma of the pylorus with secondary dilatation of the stomach.

Mayo Robson,* Tuffier and Marchais,† Thomas,‡ Page,§ Villard,‖ and others have drawn attention to pyloric obstruction due to adhesions of pericholecystitic origin.

These cases are frequently recognised during the course of operations on the gall-bladder for cholelithiasis. In many of the cases the symptoms come on very gradually and a considerable time after definite symptoms of gall-stones, so that their clinical relationship is very much obscured.

In a few of the cases hæmatemesis has been recorded, thus making the resemblance to primary gastric disorder even more definite.

When dieting and thorough medical treatment fail to relieve these cases of pyloric stenosis due to adhesions set up by calculous cholecystitis and the patient's life is made a burden by the continual pain and invalidism, exploratory laparotomy is justified.

Dr. Fütterer, of Chicago, has kindly sent me photographs of the gall-bladder in a case where old adhesions between a gall-bladder containing calculi and the pylorus were the means of conveying carcinoma from the pylorus to the gall-bladder.

In cases where a gall-stone has ulcerated into the duodenum the cicatricial contraction which follows may give rise to stricture of the duodenum and so to obstruction.** In some instances adhesions due to past cholecystitis may form bands which lead to constriction of the colon or of the small intestine and so produce acute intestinal obstruction.

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* Mayo Robson: Trans. Clinic. Soc., vol. xxvii, p. 1, 1893–4. Diseases of Gall-bladder and Bile-ducts, 1st ed., p. 73, 1897.

† Tuffier and Marchais: Rev. de Chirurg., Feb., 1897.

‡ Thomas: Rev. Méd. de la Suisse Romande, Jan., 1897

§ Page, F.: Brit. Med. Journ., 1897, vol. i, p. 205.

‖ Villard: Lyon Médical, 1902, p. 737.

** Labadie-Lagrave and Magdelaine: Journ. des Praticiens, June 25, 1898.

Niles * reported a case of stenosis of the hepatic flexure by pericholecystitic adhesions which was cured by dividing the adhesions and removing 60 small calculi from the gall-bladder.

Adhesions may be formed between the gall-bladder and the vermiform appendix as the result of inflammation of the gall-bladder. This may explain the fact that cholelithiasis often gives rise to pain suggesting appendicitis.

(B) **Results of Inflammation in the Cystic Duct.**—The impaction or passage of a calculus, especially an angular one, along the cystic duct may set up severe inflammatory changes, ulceration, and subsequently cicatricial contraction of the duct. In some cases inflammatory adhesions around the cystic duct may involve and lead to constriction of the neighbouring common hepatic and common bile-ducts. A calculus when impacted may lead to ulceration and bulging of the walls of the duct, so that the calculus becomes encysted in a diverticulum of the cystic duct. When so placed, the calculus may exert pressure on the cystic duct, as in a case reported by W. W. Cheyne,† or possibly on the common hepatic duct.

In a woman who died of bronchitis in St. George's Hospital the liver was very freely movable and showed evidence of tight lacing. The neck of the gall-bladder was long, and just at the commencement of the cystic duct there was a recess containing a gall-stone (*vide* Fig. 97). The gall-bladder was not dilated, and bile could easily be driven from the gall-bladder into the duodenum.

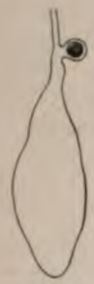

FIG. 97.—GALL-BLADDER WITH ELONGATED NECK AND DIVERTICULUM AT COMMENCEMENT OF CYSTIC DUCT CONTAINING A CALCULUS.

The process of ulceration may lead to the calculus working its way out of the duct and giving rise to a localised abscess in the immediate neighbourhood.

(C) **Inflammation and Infective Changes in the Common Bile-duct.**—The inflammation of the common bile-duct associated with the presence of a gall-stone may possibly be an extension of the cholecystitis which originally drove the calculus out of the gall-bladder, but probably in most cases the presence of the calculus favours an ascending infection of the common bile-duct from the duodenum.

Calculi in the common duct may set up chronic or intermittent inflammation, which is described below in detail as intermittent hepatic fever. It may give rise to ulceration of the duct and to perforation and the formation of a local abscess, or to suppurative cholangitis (*vide* p. 663) and multiple abscesses in the liver.

INTERMITTENT HEPATIC FEVER.

Synonym: Recurrent Hepatic Fever.

A characteristic result of calculi in the common bile-duct is a group of symptoms collectively described as intermittent hepatic fever. Its clinical features were first noted by Charcot,[*] but have been especially insisted upon by Osler,[†] and are now thoroughly well recognised.

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* Niles, H. D.: Annals of Surgery, part cxi, p. 344, March, 1902.

† Cheyne, W. W.: King's College Hospital Reports, vol. iii, p. 94.

Anatomically the calculus "floats" near the lower end of the common bile-duct, which is often greatly dilated. The calculus is movable, and is spoken of as exerting a ball-valve action (Osler,[‡] C. Fenger[§]). In many cases the dilatation of the duct around and above the gall-stone, which often lies in a pathologically dilated ampulla of Vater, allows bile to trickle past into the duodenum, so that jaundice may be transient, intermittent, or if at one time marked, may gradually pass away. There may, in fact, be no jaundice at all.

Griffon[‖] records 4 cases and Bernard[**] one where a calculus just above the biliary papilla existed without any jaundice.

The gall-stone often bulges the biliary papilla out as a projection in the duodenum. The common and other bile-ducts are dilated, often very greatly, and their walls thickened, but the mucous membrane, though inflamed, is usually free from ulceration. The liver often shows adhesions over its convexity, due to past attacks of perihepatitis. The intra-hepatic bile-ducts may be dilated, and from pericholangitis there is an increased amount of fibrous tissue around them with some atrophy of the liver substance; this constitutes the condition often described as obstructive biliary cirrhosis.

The gall-bladder is usually small, thickened, and contracted from past cholecystitis in accordance with Courvoisier's[††] well-known law that in jaundice due to gall-stones the gall-bladder is small, whereas in icterus due to the pressure of a growth on the ducts the gall-bladder is distended. There are frequently adhesions between the gall-bladder and the adjacent viscera, especially the omentum, stomach, and the transverse colon. There may be no gall-stones in the gall-bladder, but in some instances it contains a number of calculi. The head of the pancreas tends to be enlarged from chronic interstitial pancreatitis.

There is infective catarrhal inflammation of the common bile-duct.

Charcot originally regarded the fever as due to absorption of poisons from the bile-ducts. Netter and Martha,[‡‡] Abbott, and Pick[§§] have found micro-organisms, especially the colon bacillus, in the ducts. Budd[‖‖] drew an analogy between urethral fever following catheterization and intermittent hepatic fever, while Murchison and Ord[***] regarded the fever as merely the reflex result of irritation exerted by the calculus.

The striking intermissions in the symptoms may possibly depend on the micro-organisms which have set up acute catarrhal swelling of the mucous membrane of the duct and biliary obstruction, passing away into the duodenum. Or, on the other hand, periodic intervals of immunity may be developed with the result that the symptoms disappear, only to reappear when, immunity being exhausted, the micro-organisms, which in the interval, though present, have remained latent, set up a fresh and acute cholangitis.

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[*] Charcot: Leçons sur les Maladies du foie et des Voies biliaires, p. 178, 1877.

[†] Osler: Johns Hopkins Hospital Reports, vol. ii, 1890. Lancet, 1897, vol. i.

[‡] Osler, W.: Medical Times and Gazette, July 31, 1881, p. 111.

[§] Fenger, C.: American Journal Med. Sciences, vol. cxi, p. 125, Feb., 1896.

[‖] Griffon: Bull. Soc. Anat. Paris, July, 1896, p. 513.

[**] Bernard: Ibid., p. 510.

[††] Courvoisier: Beiträge zur Pathologie u. Chirurg. d. Gallenwegen, 1890.

[‡‡] Netter and Martha: Archiv de Physiolog. norm. et path., 1886, p. 7.

[§§] Pick: Brit. Med. Journ., 1898, vol. i, Epitome, No. 229.

[‖‖] Budd: Diseases of the Liver, 2d ed., p. 376, 1857.

[***] Ord, W. M.: Brit. Med. Journ., 1887, vol. i, p. 496.

Clinical Picture.—The symptoms may come on many years after the original attack of cholecystitis which gave rise to the gall-stone, and there may be an interval lasting for years, with freedom from symptoms, or there may be recurrent attacks of biliary colic eventually terminating in intermittent hepatic fever.

W. Moore * reported a case in a woman aged fifty-four who first had jaundice when nineteen years old. For twenty-five years she had had yearly attacks of biliary colic, which recently had been accompanied by jaundice and shivering. Recovery followed removal of a calculus from the common bile-duct and 21 calculi from the gall-bladder.

The clinical aspect of these cases may be summed up in the occurrence of ague-like attacks of pain, fever, rigors, and increase in the jaundice, while in the intervals the patients are fairly well and even able to live their ordinary lives. The disease may continue for years, but eventually may terminate in suppurative inflammation of the ducts, the liver, or in the neighbourhood of the calculus.

The attacks, which sometimes closely resemble ague in their periodicity, are accompanied by fever, the temperature going up as high as 103°, rigors, and sweating. The pain is felt in the region of the liver and epigastrium, and may be as severe as that of ordinary biliary colic and necessitate relief by hypodermic injection of morphine. There may be tenderness in the back, close to the tenth dorsal spine on the right side. Jaundice, which is usually present in a slight degree in the intervals, becomes more intense and may be accompanied by itching of the skin. Vomiting is often present during the attack, and dyspepsia and gastric pain from adhesions between the gall-bladder and stomach are frequently troublesome. The liver may be somewhat enlarged and tender during an attack, but the gall-bladder cannot be felt. The spleen is usually palpable during the attacks. Examination of the blood shows that there is a leucocytosis during the attack, but not in the intervals. (Pick.†)

Complications.—Inflammation and ulceration of the common bile-duct in rare instances lead to cicatricial contraction of the duct. Examples of this curiously infrequent sequela are given on page 653 (Simple Stricture of the Ducts).

Kehr ‡ records a case where complete obliteration of the common bile-duct at its junction with the cystic duct was due to this cause.

The inflammation may be acute and lead to widespread suppurative cholangitis throughout the liver. This unfortunate result is described on page 663.

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* Moore, W.: Intercolonial Med. Journ. of Australasia, Aug. 20, 1899.
† Pick, E.: Brit. Med. Journ., 1898, vol. i, Epitome, No. 229.
‡ Kehr: Diagnosis of Gall-stone Disease, American translation, p. 48.

Diagnosis.—The periodicity of the febrile attacks may closely imitate malaria, but there is no reaction to quinine and the malarial parasite is not found in the blood. The presence of jaundice in the intervals and its intensification during the attacks should always suggest cholelithiasis. The diagnosis of gall-stones by *x*-rays cannot be relied upon, as no shadow may be obtained from them. Probably a good deal depends on the experience of the radiographer. A negative result is of no value.

It is important to distinguish the condition from suppurative inflammation of the bile-ducts, which, as has been pointed out, may supervene in intermittent hepatic fever. In suppurative cholangitis the fever is much more continuous, the paroxysms are more frequent, and intervals of comparatively good health do not occur; the patient is much worse, the liver is more enlarged, the gall-bladder may be palpable, while the jaundice is not so marked.

In hepatic abscess the fever is continuous, the liver is more enlarged, and leucocytosis, if present, is constant and does not pass away as it does in intermittent hepatic fever.

In malignant disease the liver is more enlarged and the course of the disease is more rapid and not accompanied by periodic attacks of fever and pain. In malignant disease pressing on the ducts, as in carcinoma of the head of the pancreas, the jaundice is deep and the motions are devoid of bile. The gall-bladder is generally distended and the temperature is not raised.

From chronic cholangitis due to infection of the ducts with micro-organisms of no great virulence the diagnosis is difficult, but the pain and intermittent fever are more severe and prominent in the cases complicated by cholelithiasis.

Hypertrophic biliary cirrhosis in rare instances comes on acutely and might imitate a calculus passing into the duct; the periodic attacks of fever, pain, and increased jaundice are much less severe in biliary cirrhosis; further, splenic enlargement is a prominent feature in biliary cirrhosis, and is practically absent in the intervals between the attacks in intermittent hepatic fever.

The prognosis is rather bad, as suppuration may supervene, as already pointed out, in the bile-ducts, the liver itself, or in the neighbourhood. The outlook is much better if the cases are submitted to operation and the stone or stones removed from the common bile-duct. In 10 cases tabulated by Osler,* spontaneous recovery occurred in five.

Treatment.—In cases where the attacks occur at considerable intervals medical treatment should be tried. The patient should take a light, digestible diet, avoid stimulants, and keep the bowels open. The dieting of cases with gastric pain is often very disappointing, a result which can hardly be wondered at since the pain and gastralgia depend in some degree on the adhesions around the pylorus. Carlsbad water at home, or better a cure there or at Neuenahr, Kissingen, Salzschlirf, Homburg, is advisable, and it is well to increase the flow of bile over the calculus in the hope of dissolving its surface sufficiently to allow it to slip into the duodenum.

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* Osler: Lancet, 1897, vol. i, p. 1319.

For the pain hot applications, fomentations, or poultices may be tried, but in many cases morphia is required and there is the danger that the habit may be acquired. Antipyrin and phenacetin may be tried, or a mixture containing belladonna and spiritus chloroformi may be given to allay spasm. Turpentine and ether have been given with the same object. With the exception of morphia, these measures often fail. Massage is unsafe, and olive oil by the mouth of no real good so far as removal or solution of the calculus is concerned. If no improvement follows medical treatment, operative measures should be advised before the patient loses too much flesh or gets deeply jaundiced, as these conditions render the operative interference dangerous.

Operative interference should not be delayed when it becomes clear that medical treatment is unsuccessful, as there is always the possible danger that suppurative cholangitis may supervene. In addition long-continued inflammation of the ducts may eventually lead to fibrotic and atrophic changes in the liver, while the irritation of other calculi in the gall-bladder may lead to primary carcinoma there. In cases of long standing dense adhesions form around the gall-bladder and ducts and make operative interference both more difficult and more dangerous.

The most radical and effective treatment is laparotomy and removal of the stone from the common duct. It is probable that in most cases removal of the gall-bladder, unless it is entirely shrivelled up, should also be carried out, so as to avoid any possibility of recurrence. The following case illustrates the features of the disease and its successful surgical treatment:

A lady aged fifty-seven had an attack of biliary colic with fever in May, 1902, from which she recovered and went in the following month to Buxton, where the pain suddenly returned while undergoing abdominal massage. In the middle of September she had another attack of jaundice, pain, and fever lasting three weeks; after a short interval of fair health pain recurred and was more or less constant from the end of November until January, 1903, when she was seen in consultation with Dr. Swan and operation advised for a gall-stone in the common duct. The liver was not enlarged; the gall-bladder could not be felt. There was tenderness over the common bile-duct, and pain in the epigastrium. There was a slight degree of jaundice and the temperature oscillated. The pain necessitated morphia injections. The history showed that twenty-five years ago, after the birth of a child, she had had an attack of severe pain like gall-stone colic. On January 17th Mr. Mayo Robson operated and removed a gall-stone from the lower end of the common bile-duct by pressing it into the duodenum and incising the intestine. The gall-bladder was shrivelled up and united by very old and firm adhesions to the duodenum and colon. Its mucous membrane was removed according to Mayo's method. The common bile-duct was much dilated. The operation was rendered very difficult by the extensive adhesions. There was a rudimentary Riedel's lobe. The patient recovered without a bad symptom.

Probably in some cases operation short of this may do good; mere manipulation of the ducts may drive a softened stone into the duodenum and effectually remove it.

A woman aged fifty-four who had had about 20 attacks within the year came under my care in 1896 in St. George's Hospital. During an attack the temperature went up to 104°, jaundice became more marked, bile appeared in the urine, and there was marked tenderness over the common bile-duct. Mr. Sheild explored the abdomen, broke down adhesions around the common bile-duct, which felt thickened, but did not open the duct, as no calculi were palpable. After this the patient remained free from any further attacks.

Extension of Inflammation and Infection to the Pancreas.—Gall-stones in the common duct, especially when in their usual situation, viz., the lower end, readily give rise to catarrhal inflammation of Wirsung's duct of the pancreas. In this manner acute or chronic pancreatitis may be set up.

Thirty-two cases of acute pancreatic lesions, such as hæmorrhage, suppuration, acute pancreatitis, have been collected by Opie * in which gall-stones were present. He concludes that with few exceptions the gall-stones caused the pancreatic disease. I had previously called attention, though on a much smaller number of cases, to the production of pancreatitis by cholelithiasis.†

The production of suppuration in the pancreas by calculi in the common bile-duct was described in 1883 by Norman Moore.‡ The following case illustrates this point:

A man aged sixty-three, who had had an attack of jaundice and abdominal pain five years before, was seized with abdominal pain a week before his death. He was admitted to St. George's Hospital in a jaundiced, drowsy, and exhausted condition. His temperature was 101°, there was tenderness in the upper part of the abdomen, and he sweated profusely, without any shivering. He died from exhaustion within twenty-four hours of admission. At the autopsy there were three large crumbling calculi in the common bile-duct, which was dilated to the size of one's thumb and had a granular, thickened condition of its mucous membrane. The cystic duct was dilated, there was an ulcer in the fundus of the gall-bladder, which contained bile-stained mucopus but no calculi. The intra-hepatic ducts were slightly dilated and showed pericholangitic fibrosis, but there was no suppuration. The pancreatic duct contained dirty pus and there were spots of suppuration in the pancreas.

As a result of pancreatitis, infection of the peritoneum of the lesser sac of the peritoneum—the omental bursa of American writers—may occur. The inflammation of the peritoneum in the lesser sac leads to closure of the foramen of Winslow and to an inflammatory exudate. Cholelithiasis may thus set up a peripancreatic effusion in the lesser sac, the contents being either serous or purulent. Many so-called pancreatic cysts are probably of this nature.

The following case is of interest in this connexion:

A man aged twenty-five years was seized two weeks before his death with vomiting, which persisted until his death, and pain, never very acute, in the lower part of the abdomen. He had never had jaundice, a blow on the abdomen, or any serious illness. An indistinct tumor was felt in the left hypochondrium, with the stomach resonance above it. At the autopsy there were 59 small calculi in the gall-bladder and one in the cystic duct, which was very long and joined the common hepatic duct, ¾ inch above the biliary papilla. The cystic duct was inflamed, and it seemed possible that inflammation had spread from it to the pancreas. There was a localised effusion distending the lesser sac of the peritoneum into a cyst as large as one's head, the foramen of Winslow being closed. The fluid contained a fat-splitting ferment. The pancreas showed acute pancreatitis under the microscope. There were scattered islands of fat necrosis all around the cyst. This peripancreatic cyst was evidently secondary, just as pleurisy is to pneumonia, to acute inflammation of the pancreas, which in its turn was associated with cholelithiasis.*

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* Opie: American Journ. of the Medical Sciences, vol. cxxi, p. 27, Jan., 1901.

† Rolleston: Trans. Path. Soc., vol. xlix, p. 149, 1898.

‡ Moore, N.: Trans. Path. Soc., vol. xxxiii, p. 186.

More or less chronic pancreatitis from extension of inflammation from the common bile-duct *via* Wirsung's duct is probably a frequent accompaniment of calculi in the lower part of the common bile-duct. The head of the pancreas may thus become so hard that when felt during the course of an operation for gall-stones the surgeon may assume that there is malignant disease of the head of the pancreas and abandon the operation. The inflammatory changes thus started may progress, even though the calculi which caused it have passed into the duodenum. (Mayo Robson,† Barling.‡) Subsequently the enlarged head of the gland undergoes atrophy from cicatricial contraction of the newly formed fibrous tissue, and imitates a hard, slowly growing carcinoma of the head of the pancreas by compressing the common bile-duct and producing chronic jaundice.

The treatment of such cases is to establish free drainage for the gall-bladder; if this is kept up for some time, the condition of the pancreas will improve. It seems safer and better to drain the gall-bladder externally and not to do cholecystenterostomy.

Inflammatory Effects of a Calculus in the Ampulla of Vater.—A calculus in the diverticulum Vateri often obstructs the main pancreatic duct, but as there is usually a communication in the pancreas between the main duct and the accessory or Santorini's duct, the pancreatic secretion is not prevented from entering the duodenum. But as the result of continued chronic pancreatitis, cicatricial contraction may result and compress both the ducts, giving rise to retention of the secretion, dilatation of the ducts, and sometimes to the formation of cysts in the gland. The chronic interstitial pancreatitis which results from obstruction of the ducts very seldom destroys the islands of Langerhans, and glycosuria and diabetes therefore hardly ever result. (Opie.§)

Pylephlebitis.—Inflammation of the bile-ducts may give rise to suppurative pylephlebitis. The inflammation may spread to the main trunk of the portal vein or to its intra-hepatic branches. In some instances the infection may spread to the portal vein by the lymphatics or by the small veins of the bile-ducts which open into the branches of the portal vein. This subject is fully discussed under the causation of pylephlebitis. (*Vide* p. 71.)

BILIARY FISTULA.

Abnormal passages between the gall-bladder and bile-ducts and other viscera or the outside of the body are in the great majority of instances due to gall-stones and inflammatory processes accompanying them.

External fistulæ may result from other causes, such as operations on the gall-bladder and ducts, or on hepatic abscesses and hydatid cysts, while an internal fistula between the gall-bladder and the colon may depend on malignant disease. It is worthy of note that while gall-stones most commonly give rise to a fistula between the gall-bladder and duodenum, malignant disease of the gall-bladder is much more prone to set up a fistula between the colon and the gall-bladder than between the duodenum and the gall-bladder. The following remarks on biliary fistulæ refer to those associated with calculi.

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* Rolleston: Trans. Path. Soc., vol. xlix, p. 145.

† Mayo Robson: Lancet, 1900, vol. ii, p. 236.

‡ Barling, G.: Brit. Med. Jour., 1900, vol. ii, p. 1766.

§ Opie, E. L.: Jour. Exper. Med., vol. v, p. 397, 1901.

External or Cutaneous Biliary Fistulæ.—Suppuration in the gall-bladder may eventually discharge through the abdominal walls. This is the commonest recognised form of biliary fistula, probably because its presence is so manifest that it cannot be overlooked.

Naunyn[*] collected 184 examples out of a total of 384 biliary fistulæ due to cholelithiasis, the next most frequent form of fistula being that between the gall-bladder and duodenum (108).

The communication between the gall-bladder and the opening in the abdominal wall is often by a long fistulous tract which may be tortuous and difficult to follow. The fistula may be the opening of an abscess formed in the neighbourhood of the gall-bladder or may lead directly into the cavity of the suppurating gall-bladder.

External biliary fistulæ usually open near the umbilicus; this depends partly on the vicinity of the gall-bladder and partly on the fact that the falciform ligament seems to direct the suppurative process in this direction. Not uncommonly the opening is in the right hypochondrium. In rare instances there may be a discharging abscess in the right iliac fossa which imitates an appendicular abscess. The following case illustrates this point :

Gibson[†] explored a spontaneous sinus in the right iliac fossa, ¾ inch below and 2½ inches internal to the anterior-superior spine of the ilium, and removed 52 calculi, after which the fistula healed.

In very rare instances a biliary fistula may be established in the thigh. Porges[‡] has recorded the discharge of gall-stones from a fistula in this situation.

Fistulæ Between the Biliary and Gastro-intestinal Tracts.—In many instances where this condition is found after death there have been no clinical manifestations of the process, such as intestinal obstruction from a large gall-stone, or the passage of a calculus in the fæces, and its existence has not been suspected during life. A fistula may be suspected when a large calculus is passed by the bowel, but this often occurs when no absolute proof of a fistula is forthcoming.

In 111 cases where a large calculus, viz., one the size of a nut, was passed by the bowel, the method by which it gained entrance into the bowels was quite unknown in 69. (Le Roy.[§])

Duodenal fistulæ are the most frequent. In a list of 384 biliary fistulæ due to cholelithiasis the duodenum was involved in 108. (Naunyn.[‖])

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[*] Naunyn: Cholelithiasis, p. 143.
[†] Gibson, J. H.: Philadelphia Med. News, Jan. 19, 1901.
[‡] Porges: Wiener klin. Wochen., 1900, S. 597.
[§] Le Roy, C.: Thèse Paris, No. 474, 1902.
[‖] Naunyn: On Cholelithiasis, p. 143. Translation New Sydenham Soc.

As a rule, there is a communication between the fundus of the gall-bladder and the duodenum, but in a certain number of cases a calculus ulcerates through the walls of the common bile-duct into the first part of the duodenum, above the biliary papilla.

Cholecystoduodenal Fistulæ.—This was the form present in 93 out of the 108 cases mentioned above. The fundus of the gall-bladder communicates with the first part of the duodenum. The process of ulceration may give rise to severe gastro-intestinal hæmorrhage. Such cases may very easily be misinterpreted and regarded as examples of simple gastric or duodenal ulceration. In some instances cicatrisation of the fistulous communication may lead to stricture of the duodenum and to symptoms of pyloric obstruction. Dense adhesions between the gall-bladder and the duodenum may imitate malignant disease even when the parts are exposed in the course of an exploratory laparotomy. The mucous membrane around the fistulous opening into the duodenum may become extensively ulcerated and set up persistent vomiting; this may occur without any cicatricial stenosis of the duodenum or pylorus.

A calculus may ulcerate out of the gall-bladder, but fail to pass into the duodenum, and may set up so much cicatricial contraction around the duodenum that obstruction results. A case of this kind is reported by Labadie-Lagrave and Magdelaine.* Occasionally an abscess formed around a gall-stone which is ulcerating out of the gall-bladder or common bile-duct discharges in several directions and a complicated fistula results, with openings into the duodenum, stomach, and gall-bladder.

A woman aged fifty-four years died in St. George's Hospital after removal of the right big toe. She had diabetes of pancreatic origin and was jaundiced. The gall-bladder was shrivelled up on a gall-stone, and communicated by a fistula with the first part of the duodenum. There was a soft, crumbling calculus the size of a pigeon's egg in the lower part of the common bile-duct. Near this calculus, but not in actual continuity, there was an abscess, partly in the head of the pancreas and partly in the lesser omentum and left lobe of the liver. This abscess communicated by two small openings with the duodenum, and by two more fistulæ with the stomach on its posterior wall. The pancreas was markedly fibrotic.

Choledochoduodenal Fistula.—A communication between the common bile-duct and the first part of the duodenum is probably commoner than is believed. Naunyn points out that in some cases where the calculus is seen projecting into the duodenum the orifice is not the biliary papilla, as is too often assumed, merely because there is an opening there, but a fistulous passage. Naunyn thinks it not improbable that in reality fistulæ between the duodenum and the common bile-duct are as common as those between the duodenum and gall-bladder. But of his 108 collected cases of duodenal fistulæ 15 were between the common duct and the duodenum, and the remaining 93 between the gall-bladder and the duodenum.

Biliary Gastric Fistulæ.—Although duodenal fistulæ are common, communications between the stomach and biliary tract are very rare, and when they do occur, are in some instances due to an abscess, arising in connexion with the gall-bladder or ducts, opening into the stomach and also into the duodenum or colon, or both, as in a case reported by Voelcker.[*]

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* Labadie-Lagrave and Magdelaine: Journ. des Praticiens, June 25, 1890.

Naunyn[†] quotes 12 gastrobiliary fistulæ, 8 of which were between the gall-bladder and 4 between the ducts and the stomach. In a recent case of Nicholls'[‡] the patient was a woman aged eighty-five. In a complicated case reported by Lejonne and Milanoff[§] there was a communication between the stomach and the gall-bladder, and a second fistula between the common bile-duct, which contained a calculus, and the first part of the duodenum. The gall-bladder showed primary carcinoma, but the fistulæ probably depended on cholelithiasis. The patient was a woman aged eighty-seven years. Cholecystogastric fistulæ due to gall-stones have also been recorded by Ochsner[‖] and Snively.[**]

A cholecysto-gastric fistula may be brought to light in separating dense adhesions during an operation in cases where no symptoms of the fistula existed.

In a woman aged sixty who had had attacks of gall-stone pain for fifteen months, lately very frequently, followed by slight jaundice and constant dyspepsia with frequent vomiting and loss of flesh, Mayo Robson[††] found the stomach and gall-bladder firmly adherent. On separating the adhesions a fistula between the gall-bladder and stomach was found. The gall-bladder contained calculi; the patient made a good recovery.

Vomiting of gall-stones has been thought to be good evidence of a gastro-biliary fistula, but there seems to be no convincing reason for this belief, for if bile can be regurgitated into the stomach, as it commonly is in vomiting, small calculi should be so too. But when, as extremely rarely happens, a large calculus is vomited, the probabilities are that a gastro-biliary fistula exists.

Thompson[‡‡] recorded the case of a woman aged ninety-four who vomited a calculus the size of a nutmeg. Jeaffreson[§§] quoted a case where a large calculus was vomited and after death the stomach was found adherent to the gall-bladder. In 12 cases in which gall-stones were vomited there was only one in which a gastro-cholecystic fistula was shown to exist (Murchison[‖‖]). Mayo Robson,[***] Nicholls,[†††] Kellett Smith and Bailey,[‡‡‡] Crooke,[§§§] and others have reported more recent cases in which gall-stones were vomited.

Cholecystocolic Fistulæ.—A fistulous communication between the biliary tract and the colon is less frequent than one involving the duodenum as the result of cholelithiasis.

Naunyn[‖‖‖‖] gives 49 examples of fistulæ between the gall-bladder and the colon and one between the common bile-duct and the colon.

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[*] Voelcker: Trans. Path. Soc., vol. xlvi, p. 78, 1895.

[†] Naunyn: On Cholelithiasis, p. 143. Transl. New Sydenham Soc., 1892.

[‡] Nicholls: Montreal Med. Journ., Nov., 1898.

[§] Lejonne et Milanoff: Bull. Soc. Anat., 1900, p. 33.

[‖] Ochsner: Annals of Surgery, vol. xxxv, p. 712, 1902.

[**] Snively: Journ. American Medical Association, April 11, 1903, p. 963.

[††] Mayo Robson: Brit. Med. Journ., 1903, vol. i, p. 185.

[‡‡] Thompson: Trans. Path. Soc., vol. xii, p. 129.

[§§] Jeaffreson: Brit. Med. Journ., May 30, 1868, vol. i, p. 531.

[‖‖] Murchison: Diseases of Liver, 1885, p. 548.

[***] Mayo Robson: Lancet, 1897, vol. i, p. 1526.

[†††] Nicholls, A. G.: Montreal Med. Journ., Nov., 1898, p. 829.

[‡‡‡] Kellett Smith and Bailey: Liverpool Medico-Chirurg. Journ., p. 74, 1902.

[§§§] Crooke: Ibid.

[‖‖‖‖] Naunyn: On Cholelithiasis, p. 143.

As an indirect result of gall-stones, viz., from carcinoma of the gall-bladder, a fistulous opening into the colon may result. In nine cases of cholecystocolic fistulæ mentioned by Murchison 6 were associated with carcinoma of the gall-bladder.

As a rare sequela of a cholecystocolic fistula fæces may pass into the gall-bladder and set up suppuration in the liver.

This is exemplified in the following case, under the care of my colleague, Dr. Ewart, in St. George's Hospital. A woman aged thirty-one years had had jaundice, without any definite biliary colic, for one and one-half years before her death; the jaundice varied from time to time, but became very dark before death. She was thought to have malignant disease, and an exploratory operation was performed, but it was impossible to do anything. At the autopsy the gall-bladder had ulcerated into the colon, and the parts around were firmly matted together by dense adhesions. There were gall-stones and fæces in the gall-bladder, the right hepatic duct contained fæcal material, and there were multiple abscesses in the liver. (*Vide* coloured plate 7.)

Fistulæ Between the Biliary Tract and the Small Intestine.—A direct communication between the gall-bladder or ducts and any part of the small intestine except the duodenum is most exceptional, and hardly any cases are on record. The small intestine is, from its position, less likely to become adherent to the gall-bladder, and its free mobility further protects it.

Naunyn * refers to two cases, one in which the jejunum (Gaston), and the other in which the ileum, communicated with the gall-bladder.

Results of the Passage of Calculi into the Intestines.—A calculus may obstruct the lumen of the bowel and mechanically give rise to intestinal obstruction. This condition is described on page 742. It may set up inflammation of the wall of the bowel, and may thus give rise to the formation of a diverticulum in which the calculus is contained. The wall of the bowel may be so damaged that it undergoes gangrene. In most exceptional instances a small gall-stone has been described as passing into the vermiform appendix. As the result of ulceration between the gall-bladder and duodenum or colon cicatricial contraction and stricture of the bowel may occur. Cicatrisation of a fistula is, however, a rare event (Naunyn †) or is rarely recognised at the autopsy.

Bronchobiliary Fistulæ.—In 35 cases collected by Graham ‡ of this condition, including 24 of Courvoisier's, 19 were due to cholelithiasis, 11 to hydatids, 2 to ascarides; in 2 the cause was not forthcoming, and in one it was referred to traumatism. As cholelithiasis is far the most frequent cause of bronchobiliary fistulæ, a general account of the condition will be given here. Gall-stones may give rise to a bronchobiliary fistula in several ways:

(*a*) Gall-stones in the common duct set up infective cholangitis and an abscess in the liver which perforates the diaphragm, and after setting up adhesions between the diaphragm and the base of the lung, ruptures into the latter; or the liver abscess may perforate first into the pleura and subsequently into the lung.

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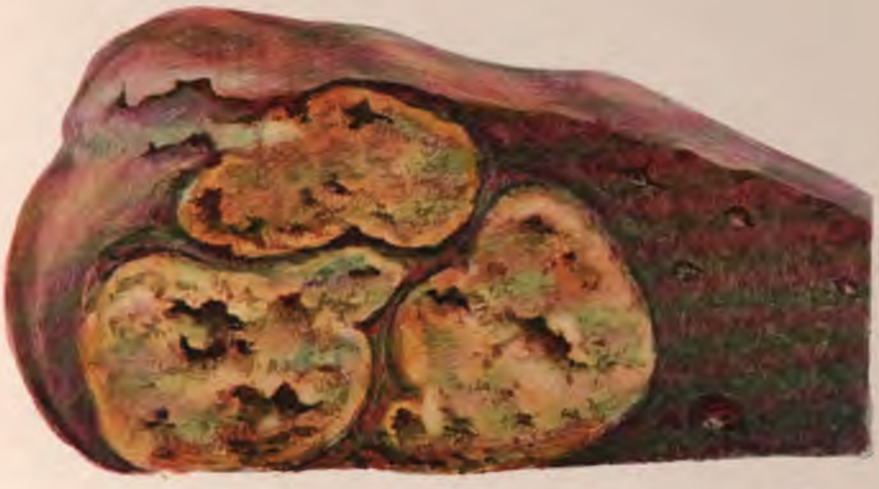
* Naunyn: On Cholelithiasis, p. 148.

† Naunyn: On Cholelithiasis, p. 150.

‡ Graham, J. E.: Trans. Assoc. American Physicians, vol. xii, p. 247.

PLATE 7.



Section of Liver Showing Abscess due to Infection of the Bile-ducts in a Case of Cholecystocolic Fistula from Cholelithiasis.

(*b*) Intra-hepatic calculi may give rise to a similar sequence of events.

(*c*) A calculus may ulcerate out of the gall-bladder or ducts, and set up an intra-peritoneal abscess which perforates the diaphragm and either opens into the lung direct or first into the pleura and subsequently into the lung.

(*d*) A suppurating gall-bladder associated with cholelithiasis may set up a subphrenic abscess which perforates the diaphragm and eventually opens into the lung.

(*e*) In very rare cases, as in Mandard's,* the gall-bladder may perforate directly through the diaphragm into the lung.

Symptoms.—Irritating cough may be accompanied by orthopnœa and the expectoration of large quantities of bile, sometimes almost pure. Graham speaks of expectoration of as much as 700 c.c. of bile in the twenty-four hours. In a few cases the patients have coughed up biliary calculi.

Signs.—There may be dulness in the right inframammary and axillary regions, extending back for a variable extent, the breath-sounds over this area being coarse and accompanied by râles. On the other hand, there may be no dulness on percussion, and merely the signs of bronchitis. When the discharge of bile is free, there may be no obstructive jaundice and no bile in the urine, as in Smith and Rigby's † case.

The *diagnosis* depends on the expectoration of bile in considerable quantities. In jaundiced patients with bronchitis or pneumonia the sputum, like other excretions, is bile-stained, but the amount of bile is much less. Fragments of liver tissue may also be found in the sputum. When the existence of a bronchobiliary fistula is determined, its cause is sometimes difficult to make out; other signs of cholelithiasis, or in rare cases the expectoration of biliary calculi, would settle the diagnosis, but in many cases that recover or are not examined postmortem the cause remains doubtful.

Prognosis.—Recovery may occur spontaneously or after operative interference on the biliary apparatus. When spontaneous recovery occurs, there is, generally speaking, no liability to return of the fistula; a relapse has, however, been known to occur.

In a case reported by J. E. Graham a patient, after expectorating bile, was free for ten years from any symptoms; at the end of this time they recurred and proved fatal.

Treatment.—If the condition does not tend to pass away and undergo spontaneous cure, laparotomy, with the view of relieving the obstruction to the passage of bile into the intestine, should be undertaken; when gall-stones are removed from the common duct, the fistulous channel into the lung should heal up.

Other and Rare Forms of Fistulæ.—*Fistulæ Between the Bile-ducts Themselves.*—Naunyn,‡ who quotes 8 cases, adds that they are merely of anatomical interest.

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* Mandard: Thèse Paris, 1854. Quoted by Naunyn.

† Smith and Rigby: Brit. Med. Journ., 1903, vol. ii, p. 313.

‡ Naunyn: On Cholelithiasis, p. 149. Translation New Sydenham Soc.

Fistulæ Between Gall-bladder and the Portal Vein.—This is a very rare condition. Naunyn quotes 3 cases, but does not admit Bristowe's * case. According to tradition, there were three calculi in the portal vein of Ignatius Loyola, but Galliard † considers this doubtful, and it is probable that the calculi were really in the common bile-duct, which was mistaken for the portal vein. Ulceration of a calculus into the portal vein would, of course, tend to set up suppurative pylephlebitis.

Ulceration of the Hepatic Artery.—A communication between the gall-bladder or the bile-ducts, on the one hand, and the hepatic artery or its branches, on the other hand, leads to profuse or even fatal hæmorrhage which runs down the ducts into the alimentary canal. Most of these cases have been regarded as examples of aneurysms of the hepatic artery or its branches, rupturing into the biliary tract. But it must be remembered that ulceration of the gall-bladder or bile-ducts in cholelithiasis may erode the walls of the hepatic artery or its branches and first give rise to an aneurysmal bulging and subsequently to rupture of the vessel into the biliary tract.

According to Naunyn,‡ Lebert's case of an hepatic aneurysm rupturing into the gall-bladder was probably of this nature, while M. B. Schmidt recorded a clear case of ulceration of a bile-duct, due to a calculus, producing an hepatic aneurysm.

Fistulæ Between the Gall-bladder and the Kidneys.—This form of fistula is very rare. Courvoisier § quotes five cases. The fistulous passage is usually between the gall-bladder and the pelvis of the right kidney. Elsner ‖ has reported another case which showed a gall-stone in the pelvis of the right kidney.

Fistulæ Between the Gall-bladder and Urinary Bladder, etc.—This is a very infrequent event. Barnard,** however, refers to a number of cases. H. Faber, in 1839, wrote an octavo volume on the subject. Köstlin and Wucherer have described fistulæ, and Abt, Güterbock,†† and Hahn, biliary calculi in the urinary bladder.

A case of cholecystovaginal fistula has been reported. It is quite conceivable that an elongated gall-bladder with an abscess in connexion with it may track into the pelvis.

A communication between the *pericardium and the biliary tract* is one of the rarest fistulæ. In 1892 Naunyn only knew of one case.

Rupture and Perforation of the Gall-bladder into the Peritoneum.—It is most unlikely that a healthy gall-bladder would rupture merely from the weight of contained gall-stones, but, as a matter of fact, the gall-bladder is very seldom healthy in cholelithiasis. It may be thinned from distension, and rupture may then take place from traumatism, or as the result of sudden pressure brought to bear on the gall-bladder by contraction of the abdominal walls in violent straining, coughing, etc., or in the vigourous abdominal contractions of delivery. In such cases there may be no active inflammation or previous ulceration of the gall-bladder. If the bile is free from microbic infection, the peritoneum may be little the worse. Cases have occurred in which large quantities of bile have been removed from the abdominal cavity, but this chiefly occurs in cases when a hydatid cyst in connexion with a bile-duct ruptures into the cavity of the peritoneum. (*Vide* p. 412.)

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* Bristowe: Trans. Path. Soc., vol. ix, p. 285.

† Galliard: Médécine Moderne, Nov. 20, 1895.

‡ Naunyn: On Cholelithiasis, p. 141.

§ Courvoisier: Pathologie u. Chirurgie der Gallenwege, 1890.

‖ Elsner: Medical News (N. Y.), Feb. 5, 1898.

** Barnard, H. L.: Annals of Surgery, Aug., 1902, vol. xxxvi, p. 161.

†† Güterbock: Virchow's Archiv, Bd. lxvi, S. 273.

Usually rupture of the gall-bladder is disposed to by recent inflammation of its walls or by definite ulceration. Under these conditions the contents of the gall-bladder are infected, and if they pass into the general cavity of the peritoneum, generalised peritonitis will be set up.

In some instances, as the result of adhesions around the gall-bladder, the rupture or perforation sets up a localised peritoneal abscess, which may contain calculi, in communication with the gall-bladder. An abscess of this kind may open either externally on the surface of the body or into one, or even into several, of the abdominal or thoracic viscera, and thus give rise to fistulæ, which may be multiple and extremely complicated.

In rare instances a localised abscess is formed behind the peritoneum, the gall-bladder having become adherent to the posterior abdominal wall.

In other cases calculi may ulcerate out of the gall-bladder and be found surrounded by adhesions.

Moynihan * describes a case in which three gall-stones, each the size of a Barcelona nut, had ulcerated almost through the walls of a gall-bladder showing chronic sclerosing cholecystitis. Two of these calculi lay in pockets in the omentum and the third was almost hidden in a cavity in the liver.

TREATMENT OF CHOLELITHIASIS.

Prophylaxis.—In fat people, especially women, and after typhoid fever, influenza, malaria, and pregnancy, it may sometimes be within the medical man's power to advise a change in the patient's mode of life which will tend to prevent, or diminish the liability to, catarrhal inflammation of the gall-bladder and bile-ducts. These measures are, in the main, on the same lines as those for the general hygienic treatment of cholelithiasis in the intervals between the attacks. The points to be borne in mind are to prevent stagnation of bile in the biliary tract, and to obviate or remove any inflammatory condition of the mucous membrane of the duodenum, biliary papilla, bile-ducts, etc. Thus gentle exercise, in the fresh air if possible, short of fatigue, so as to favour the passage of bile into the intestines, is advisable. When this is not practicable, breathing exercises to increase the movements of the diaphragm and liver should be instituted. Stooping over desks and working in a cramped position must be corrected, while the use of tight corsets, belts, etc., should be discontinued. The patient should be warmly clad, so as to avoid chills. A visit to one of the spas mentioned on page 769 is a valuable precautionary measure.

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* Moynihan: Brit. Med. Journ., 1903, vol. i, p. 186.

GENERAL TREATMENT.

The general medical treatment of cholelithiasis and its various manifestations may be considered under the following heads:

To prevent stagnation of bile.

To prevent the occurrence of catarrhal inflammation of the gall-bladder and bile-ducts.

To remove catarrhal inflammation when it has appeared.

To attempt to dissolve and remove calculi from the gall-bladder and ducts.

Spa treatment.

To Prevent Stagnation of Bile.—Stagnation of bile in the gall-bladder favours infection and cholecystitis, and therefore the production of gall-stones, or if these are already present, an immediate attack of colic. It is, therefore, important that stagnation should, as far as possible, be prevented, and for this object the following methods may be adopted:

Exercise, which leads to increased movements of the diaphragm and liver and so to an increased flow of bile into the duodenum. In comparatively young and vigourous persons active exercise, rather than a "constitutional" walk, is needed. Horse exercise is perhaps the best, but bicycling, climbing, tennis, and rowing are excellent. In cases where active open-air exercise is not possible, deep respirations should be practised so as to induce vigourous movements of the diaphragm and liver, while in some cases abdominal massage is useful in increasing the tone of the abdominal muscles and the flow of bile. After pregnancy the lax condition of the abdominal wall, which favours enteroptosis, hepatoptosis, and stagnation of bile, may be met by massage to the abdominal muscles, care being taken not to bring direct pressure to bear on the gall-bladder, since cholecystitis may thus be set up.

The factor of dress, especially the corset, tight waist-bands, and heavy skirts, in constricting the lower part of the chest and preventing free diaphragmatic respiration, has been referred to in the consideration of the greater incidence of gall-stones in women (*vide* p. 717). These causes should be obviated, and the wearing of tight belts in men discontinued.

By the Administration of Food and Drink.—When food passes into the duodenum, bile is driven out of the gall-bladder into the duodenum. Meals at short intervals, therefore, are more effective in preventing biliary stagnation than larger meals at longer intervals. Kehr,* in fact, suggests that one factor which accounts for the much greater frequency of gall-stones in German women is that the wives do not share in the late suppers taken by their husbands. In addition to meals at comparatively short intervals some supper should be eaten before going to bed, and it is a good plan to have some food available, so that in case the individual wakes, a small meal may be taken during the night. The details of the diet will be considered later. (*Vide* p. 769.)

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* Kehr: Diagnosis of Gall-stone Disease, p. 70, American translation.

Though experimental results show that water cannot be considered a cholagogue, good results undoubtedly follow the taking of large draughts of hot water. Vichy, Carlsbad, or Contrexeville waters have a good effect, or hot water containing some sulphate or phosphate of soda. The action of an increased amount of water is probably complex: the bile is diluted and rendered more copious, while catarrh of the ducts and intestine is relieved. In order to get the maximum effect from water it should be taken before meals, when the stomach is empty. Thus it may be taken the last thing at night or, as is more frequently done, early in the morning. It should then be sipped in the intervals of dressing, or later in the day while walking about in a garden.

The water should, of course, not be taken in excessive quantities or too hot, otherwise dilatation of the stomach may occur. Dr. Wightwick has told me of a patient who, having some knowledge of medicine, treated himself for gall-stones by copious draughts of water as hot as he could bear, and as a result developed very acute dilatation of the stomach which nearly proved fatal.

Copious enemata of hot water have been recommended and have been thought to induce muscular contraction of the gall-bladder and expulsion of the contained bile.

Cholagogues.—Although a number of drugs have been credited with the power of increasing the secretion and flow of bile, it is now generally agreed that salicylate of soda and bile itself are the only drugs which really increase the secretion of bile. Mercury, podophyllin, iridin, rhubarb, senna, aloes, turpentine, and other drugs may increase the peristaltic contraction of the ducts and so lead to a temporary increase in the amount of bile discharged into the duodenum, but do not really augment the secretion of bile. (Rutherford and Vignal,* Mayo Robson.†)

Toluylendiamin at first increases the flow of bile, but later the bile becomes more viscid from an increased quantity of mucus in it. (Stadelmann,‡ Hunter.§) This body has only very occasionally been employed in medicine, and is dangerous from its hæmolytic or destructive action on the red blood-corpuscles and its tendency to produce inflammation of the small bile-ducts and jaundice.

Secretin, which, as Starling and Baylis‖ have shown, is manufactured in the duodenal mucous membrane and stimulates the secretion of the pancreas, also increases the secretion of bile.

Ox bile is sometimes given in capsules, but it is better to give the salts of the bile acids alone, since the bile-pigments are themselves somewhat poisonous.

Gautier** met with complete relief from attacks of biliary colic, which had extended over five years, after a prolonged course of ox bile.

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* Rutherford and Vignal: Jour. Anat. and Phys., vol. x.

† Mayo Robson: Proc. Royal Soc., vol. xlvii, p. 21, 1890.

‡ Stadelmann: Archiv f. exper. Path. u. Pharmak., 1887.

§ Hunter, W.: Journ. Path. and Bacter., vol. iii, p. 259.

‖ Starling and Baylis: Proc. Roy. Soc., 1902, vol. lxix, p. 352.

** Gautier: Rev. Méd. de la Suisse Romande, June 20, 1898.

Salicylate of soda has the advantage that it not only increases the secretion of bile, but that it acts as an intestinal antiseptic and so tends to diminish intestinal catarrh. It may be given in 10-grain doses twice or three times daily with an equal quantity of bicarbonate of soda. The most satisfactory treatment from the point of view of inducing an increased flow of bile is to give salicylate of soda combined with plenty of alkaline waters. Aspirin (acetylo-salicylic acid) may also be given, but is incompatible with bicarbonate of soda.

Chauffard * combines salicylate of soda with benzoate of soda for periods of twenty, fifteen, ten days in every month for a year or two, the duration of the course diminishing as time goes on. Iodide of potassium has been found of use in checking frequent attacks of colic. Its method of action is doubtful; possibly it may increase the mucous secretion from the walls of the biliary tract and so increase the flow of fluid through the ducts and thus relieve catarrh. It is also conceivable that, like chloroform and ether, it may diminish spasm.

The Prevention of Catarrhal Inflammation.—Indigestion and gastritis, which, by leading to gastro-duodenal catarrh, might set up catarrhal inflammation of the bile-ducts, must be treated by careful dieting, drugs, and the prevention of constipation. The food should be bland, nutritious, and eaten slowly. The condition of the teeth should be seen to, so that the food can be properly masticated, and further that there is no oral sepsis to set up gastritis. Worry and anxiety are frequent causes of dyspepsia, and in this way may be instrumental in favouring infection of the ducts and gall-bladder. Constipation and the attendant tendency to indigestion and gastro-intestinal fermentation and putrefaction should be prevented by gentle purgatives; the use of vigourous purges must be avoided, as enteritis may thus be induced. Salines, such as half a tumbler of natural Carlsbad water with a little hot water before breakfast, or one or two drachms of Carlsbad salts dissolved in hot water are useful. Phosphate of soda in drachm doses may also be given in water early in the morning. The Carlsbad salts are better borne by the stomach if a little of the infusion of quassia or cinchona is added to the draught (Stewart †). After taking the salts the patient should walk about, or better, practise systematic exercises with deep inspiratory movements so as to favour the descent of the diaphragm, and should not have any food until an hour after the draught has been taken.

To Remove Catarrhal Inflammation of the Biliary and Intestinal Tracts.—It is most important to remove inflammation of the gall-bladder, because calculi are formed as a result of catarrhal cholecystitis and are not likely to be dissolved so long as the gall-bladder is inflamed. Harley and Barrett ‡ have shown that calculi introduced into dogs' gall-bladders are dissolved by the bile when the gall-bladders are healthy, but not when cholecystitis is kept up.

The methods already referred to, by which the flow of bile is increased and the bile-passages washed down, are of use in removing catarrhal inflammation of the gall-bladder and bile-ducts. Carlsbad salts, phosphate of soda, Epsom salts in hot water, or table waters, such as Contrexeville, Homburg, etc., should be taken so as to remove catarrhal inflammation of the intestines and keep the bowels loose. Vigourous purgatives should be avoided, as they tend to set up inflammation of the mucous membrane.

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* Traité de Méd. (Bouchard, Brissaud), t. v, p. 85.

† Stewart, D. D.: American Journ. of the Medical Sciences, vol. cxxv, p. 851.

‡ v. Harley and Barrett: Journ. of Physiology, vol. xxix, p. 341, 1903.

The abdomen should be kept warm, so as to avoid chills, and in cases where there is tenderness over the gall-bladder poultices, hot packs, or fomentations, or heat by means of the thermophore, may be applied over the right hypochondrium.

A. E. Wright * has tentatively suggested that patients should be immunised against the colon bacillus, so that the cholecystitis due to colon infection should be arrested and that when this has been brought about, the calculi might gradually dissolve in the bile.

Attempts to Dissolve Calculi.—Numerous drugs have been tried and recommended with a view to dissolving calculi, but with very little, if any, success. A very famous, ancient remedy was Durande's, which consisted of a mixture of ether (♏ xv) and turpentine (♏ x) in a capsule. Although this remedy may do good by virtue of the antispasmodic action of ether or of the expulsive action of turpentine,—radically opposed as these actions are,—there is no reason to believe that the calculi in the gall-bladder are acted upon directly by the drugs. Chloroform, which has been employed as a solvent, probably acts chiefly as an antispasmodic.

Olive oil has been widely used to relieve the symptoms of cholelithiasis. It has been shown to dissolve calculi out of the body (Brockbank,† L. Scott ‡), but there is no evidence that olive oil given by the mouth, much less when injected per rectum, can act on calculi in the gall-bladder. In fact, there is a well-known fallacy about some of the good effects ascribed to the use of olive oil, namely, that the oil itself may be so digested and altered as to imitate softened calculi when passed by the bowel.

Delépine § described a case where a patient taking olive oil for cholelithiasis passed 40 round or oval bodies which were at first regarded as biliary calculi and as evidence of the success of the treatment. They turned out to be masses of crystals of fatty acids derived from the oil.

It is quite conceivable, however, that olive oil might exert a solvent action on a calculus impacted in the actual orifice of the biliary papilla. It has also been thought that fatty acids and glycerine absorbed from the bowel may reach the liver and lead to an increased flow of bile into the gall-bladder. Bile acids dissolve cholesterin, hence the more bile passes over a calculus, the better the chance of some absorption taking place. Some of the good effects of oil may be due to its soothing and antispasmodic action on the intestine. Olive oil is given in quantities of from 6 to 12 ounces a day by the mouth, but is far from a pleasant thing to take. Some writers (Chauffard, Dupre *), however, speak highly of the good effects of olive oil in cholelithiasis. Pure olive acid (Merck) and eunatrol, or pure oleate of soda, have been recommended instead of the oil. Fat and cream may also be taken in place of the oil, unless they disturb digestion.

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* Wright, A. E.: Brit. Med. Journ., 1903, vol. i, p. 1073.
† Brockbank, E. M.: Med. Chronicle, vol. xix, p. 155.
‡ Lindley Scott: Brit. Med. Journ., 1897, vol. ii, p. 798.
§ Delépine, S.: Trans. Path. Soc., vol. xli, p. 111.

Since the bile acids dissolve cholesterin, any increase in the secretion of bile, such as is induced by salicylates or by the administration of bile by the mouth, may be regarded as a means of dissolving calculi. Since proteid food increases the percentage of bile acids in the bile, meat has been regarded as an important element in the diet of patients suffering from gall-stones. As already pointed out, Harley and Barrett's experiments show that calculi are dissolved by the bile provided cholecystitis is absent. It is, therefore, important to prevent or remove inflammation of the gall-bladder.

Attempts to Remove Gall-stones.—Measures such as massage and drugs such as turpentine and purgatives which lead to muscular contraction of the gall-bladder and bile-ducts have been employed to favour the expulsion of calculi. At the commencement of a course at Carlsbad it not uncommonly happens that a patient experiences an attack of biliary colic and passes calculi. Turpentine has been recommended by Ralfe † in cases of irregular biliary colic to favour the passage of calculi. Increasing the flow of bile by salicylates and ox bile cannot be regarded as likely to drive calculi out of the gall-bladder, though their good effects in reducing catarrh of the ducts and the possibility that calculi may, as already pointed out, be dissolved, must not be forgotten. Measures intended to lead to the expulsion of gall-stones are somewhat uncertain in their action. Massage of the gall-bladder and bile-ducts in order to effect "the extrusion of gall-stones by digital manipulation" was advocated by the late Dr. George Harley ‡ in 1888, and has been widely condemned as a dangerous method of working in the dark. No doubt it might lead to the expulsion of soft calculous masses lying in the common bile-duct, but in many cases it would be quite powerless to do any good and might easily do harm by leading to rupture of an ulcerated gall-bladder or duct. If it were possible to recognise with certainty cases with soft calculous material in the common duct, gentle massage might be recommended, but, unfortunately, our methods of diagnosis are not sufficiently sure to enable us to do so, and, accordingly, massage in cholelithiasis is a haphazard and, it must be admitted, a dangerous method of treatment.

Spa Treatment.—Mineral waters dilute and increase the flow of bile and may thus lead to some degree of solution of calculi in the ducts and gall-bladder and to their ultimate discharge into the duodenum. The increased flow of bile flushes the bile-ducts and thus tends to remove infective catarrh and so to prevent the further formation of calculi and possibly to favour absorption of calculi. It is not absolutely necessary to go to a spa in order to undergo the treatment, for it can be carried out under medical advice at home, but the patient probably gains by going to the original source from the change of scene and from the influence exerted by the regular life, the régime, and the freedom from business cares and worries.

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* Chauffard, Dupre: Soc. Méd. des Hôp. Paris, Oct. 12, 1888.
† Ralfe: Lancet, 1891, vol. ii.
‡ Harley, G.: Illustrated Med. News, Oct. 20, 1888.

Carlsbad, Vichy, Marienbad, Kissingen, Homburg, Neuenahr, Ems, Bertrich, Brides, are appropriate spas on the Continent. In England Harrogate, Llandrindod Wells, enjoy some reputation, while in America Bedford, Pa., Las Vegas Hot Springs, Sharon, White Sulphur, are recommended for the treatment of gall-stones.

At Carlsbad and Vichy it not infrequently happens that calculi are passed after the course of treatment has begun; patients should, therefore, be warned that they may have a return of colic with jaundice. Neuenahr and Bertrich are less depressing than Carlsbad, while the waters at Salzschlirf, Wiesbaden, Nauheim, and Soden are sometimes recommended.

Diet.—Food should be taken at comparatively short intervals and the amount at each meal should not be large, while overeating must, of course, be prevented. As to the kind of food most suitable for patients with gall-stones, considerable divergence of opinion has been expressed. It is unnecessary to insist on the fact that the food should be digestible and not too bulky. The amount of starchy food should be much restricted, and bread should be taken sparingly and preferably as toast, while sugar must only be allowed in small quantities. Porridge and rice may be taken in moderation. It is particularly with regard to fatty food that contradictory statements have been made. Some writers believe that fats favour the production of calculi; others that fats are indicated as solvents of gall-stones. It is probable that fatty food has no particular action in dissolving calculi in the bile-ducts or gall-bladder, and that it only does harm indirectly, viz., when it gives rise to acid dyspepsia. As a general rule, fatty food should be taken in small quantities and carefully watched; when any signs of dyspepsia or fermentation appear, it should be diminished in amount, or, if need be, discontinued.

Proteid food may be taken with greater freedom and may consist of mutton, beef, game in small quantities, and vegetables containing a good deal of albumin. It has been thought that proteid food, by increasing the amount of the bile acids, may assist in dissolving cholesterin; this, however, is problematical. Alcohol is best avoided, and if required for other reasons, should be well diluted. Light claret, still Moselle, or a little whisky may be taken in this way. Beer, stout, champagne, and especially liqueurs should be forbidden. The importance of taking plenty of water before meals has already been insisted on.

SURGICAL INTERFERENCE IN CHOLELITHIASIS.

It has already been pointed out that in acute biliary colic operative interference is justifiable only when life is threatened by some extremely grave complication, such as rupture of the gall-bladder or bile-ducts with resulting peritonitis, or when, as rarely happens, concomitant acute infective cholecystitis sets up widespread peritonitis, or when signs of acute intestinal obstruction appear.

The effects of chronic or irregular cholelithiasis which require surgical interference may be arranged as follows:

(i) When there is acute inflammation in the region of the gall-bladder with the signs of *severe* localised peritonitis.

(ii) When, in a case with a history of gall-stones, there are symptoms pointing to acute perforative peritonitis, such as might be set up by perforation of the gall-bladder.

(iii) When, from the presence of fever, pain, jaundice, etc., there is evidence that severe infective inflammation of the bile-ducts has developed. Under these conditions the gall-bladder and ducts should be freely drained.

(iv) When acute intestinal obstruction occurs in patients with a history of gall-stones.

(v) When there is a large tumor constantly present in the position of the gall-bladder, such as might be due to distension of the gall-bladder by serous or mucous fluid (dropsy of the gall-bladder), by pus (empyema), or by a collection of calculi.

(vi) When jaundice in a patient with a history of gall-stones becomes chronic. The period which should be allowed to elapse after the onset of permanent jaundice varies very considerably. Hanot fixed the period at three months. Boix * shortened it to six weeks, while C. Beck † argued in favour of four weeks. If medical measures are quite ineffectual and the patient loses ground, the chance of relief from operation is certainly diminished by delay, as the liver cells are further damaged by the prolonged stagnation of the bile in the intra-hepatic bile-ducts. There is also the danger that infective catarrh may supervene in the dilated bile-ducts or in the liver. Further, the marked tendency to hæmorrhage which exists in so many deeply jaundiced patients makes operative interference difficult and dangerous. No hard-and-fast rule can be laid down as to the time which should be allowed to elapse before a patient with chronic jaundice is operated upon. The patient's condition, general nutrition, presence or absence of symptoms, and response to treatment must all be considered. If improvement occurs under medical treatment, it would obviously be unwise to adopt operative measures. As a general rule, operation should be advised earlier in poor patients whose livelihood depends on their ability to work than in well-to-do patients who can afford a cure at Carlsbad, Neuenahr, etc.

(vii) In intermittent hepatic fever, where there is a calculus in the common bile-duct which sets up recurrent attacks of fever, pain, and jaundice, medical treatment should always be given a good trial, and if the attacks become less frequent and severe and gradually disappear, there is, of course, no need for operation. On the other hand, if the attacks become more frequent or no improvement occurs, operation should be considered and should be carried out before the patient becomes too run down in strength and resistance.

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* Boix: Archiv. général. de Méd., Oct., 1901, p. 470.

† Carl Beck: The Medical Week, 1897, p. 137.

(viii) In recurrent biliary colic, without the passage of calculi in the stools, which leads to serious impairment of the patient's health and threatens to induce a condition of chronic invalidism, the question of operative interference must be considered. A poor man who cannot afford the loss of time and expense involved by a cure at Carlsbad, Neuenahr, Harrogate, etc., should be advised to submit to operation. A rich patient should be given the chance of a course of spa treatment under careful medical supervision before an operation is undertaken. An additional reason for operating in some cases is that carcinoma of the gall-bladder occurs in from 14 to 4 per cent. of all the persons with gall-stones, and that removal of the gall-stones or, if necessary, of the gall-bladder may prevent this sequela. In a case of recurrent attacks of biliary colic it would probably be safer to advise operative interference at any earlier date in patients who have a family history of carcinoma than other patients.

(ix) When, from adhesions between the gall-bladder and pyloric end of the stomach, continued and severe gastric symptoms are produced. (*Vide* p. 749.)

(x) In patients who are acquiring the morphia habit as the result of prolonged suffering operative interference is necessary to prevent the establishment of this pernicious habit.

(xi) In some cases of fistulæ, both external and internal.

For the details of the surgical operation the reader must consult the text-books on operative surgery.

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